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Original Communications

Department of Clinical Reports

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The American Heart Journal

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Original Communications

A STUDY OF THE ESOPHAGEAL LEAD IN CLINICAL ELECTROCARDIOGRAPHY*†

PART I. THE APPLICATION OF THE ESOPHAGEAL LEAD TO THE HUMAN SUBJECT WITH OBSERVATIONS ON THE TA-WAVE, EXTRASYSTOLES AND BUNDLE-BRANCH BLOCK

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IN recent years the field of clinical electrocardiography has been extended by the reintroduction of chest leads. The increased use of this type of "unconventional" lead has followed the work of Wood and Wolferth,[72] who found that the standard or indirect Leads I, II, and III sometimes fail to disclose information of diagnostic importance in heart disease. Precordial leads have also been employed in an "exploring" rôle by Wilson and his collaborators[64, 68] in cases of bundle-branch block. There can be little doubt that the utilization of such nonstandard leads has provided a clearer insight into the electrical events occurring on the anterior surface of the heart and has aided in the detection of infarcted areas in the ventricle. On the other hand, the chest leads permit of no more than inferential conclusions as to the electrical events in the left ventricle and disclose no new information with respect to the electromotive changes in the auricular muscle. It has been primarily with a view to investigating the value of the esophageal lead in exploring these regions that the present studies have been undertaken.

The use of the esophagus as a site for the derivation of action currents arising in the heart has had a considerable vogue in animal experimentation. Kraus and Nicolai[27] (p. 85), Rothberger and Winterberg,[51] Selenin,[57] and many others have made use of ano-esophageal leads in dogs. In such procedures the lead has been employed as an axial derivation and not as an exploring method in the more recent terminology of Wilson.[64]

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†Presented in abstract before the American Heart Association, Atlantic City, June 11, 1935.

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In the human subject the alimentary route was first used by Waller[60] who placed an electrode in the mouth; but, with the replacement of the capillary electrometer by Einthoven's[15] modification of Ader's[1] galvanometer, this derivation lapsed into disuse. In 1906 Cremer,[10] attracted by the desirability of a closer approach to the cardiac electrical field, reported that he had successfully placed an electrode in the esophagus behind the heart under roentgenological control. He advocated the wider use of this method inasmuch as it permitted of the closest possible approach to the heart in the normal human subject. The following quotation from his paper probably explained why his enthusiasm was not communicated to the profession at large: "Zu meinen Versuchen bei Menschen diente mir hauptsächlich ein Degenschlucker von Beruf der anodisch vorbehandelte Silberelektroden bis zu 10 cm. Lange und 1.5 cm. Durchmesser beliebig in Oesophagus zu plazieren verstand"[10] (p. 812).

In 1934 Lieberson and Liberson[30] revived the method and applied it to six normal human subjects. They used a small German silver electrode and placed it behind the heart under fluoroscopic control. Unfortunately the publication of a typical curve was unaccompanied by a detailed analysis of their material so that it was impossible to evaluate the importance of the method on the data given in their paper.

The investigations reported in the present communication have been devoted to testing the theoretical validity and practical adaptation of the method to human subjects in health and disease. The subject has been treated under two main heads. Part I has been subdivided into the following sections:

1. The application of the method: theory and technic.
2. An analysis of the normal esophageal curves from the human auricle.
3. Observations on the Ta-wave and auricular extrasystoles.
4. An analysis of the ventricular complexes of esophageal leads in normal individuals.
5. Observations on clinical cases of bundle-branch block and ventricular extrasystoles.

Part II, to be published later, is entitled "An Electrocardiographic Study of Auricular Disorders in the Human Subject by Means of the Esophageal Lead."

Part I

The Application of the Esophageal Lead to the Human Subject, With Observations on the Ta-Wave, Extrasystoles and Bundle-Branch Block

Section I. The Application of the Method: Theory and Technic

Anatomical Considerations.—As the esophagus passes downward through the thorax behind the trachea, it courses along the right side

of the arch of the aorta and then slightly backward over the root of the lung and bronchotracheal lymph nodes (Fig. 1 *A*). It then runs slightly forward, and about 1.2 to 2 cm. below the tracheal bifurcation it lies directly behind the upper pole of the left auricle (Fig. 1 *B*) in the midline of the body. In its downward course along the posterior surface of the heart (left auricle) opposite the eighth vertebra it begins to deviate to the left and lies in front of the descending aorta (Fig. 1 *C*). As it passes still farther to the left and forward to seek the

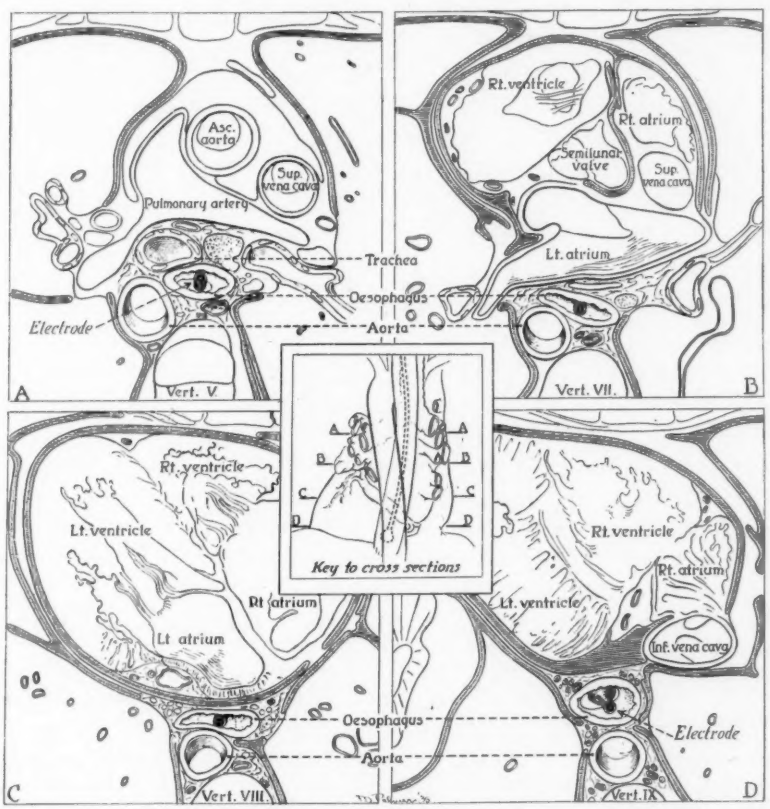

Fig. 1.—Drawings (after Eycleshymer and Schoemaker[19]) of cross-sections of the heart illustrating the anatomical relationship between the esophageal electrode and the heart at the levels indicated in the key drawing.

esophageal aperture of the diaphragm, it passes the lower pole of the left auricle and traverses the posterior or basal portion of the left ventricle (Fig. 1 *D*). Its close cardiac relationships are, therefore, with the left auricle and the left ventricle. The right auricle and the cavae lie to the right and anteriorly at some little distance from the esophagus. The right ventricle lies anteriorly and to the right.[49] Separating the esophagus from the structures enumerated are connective tissue and the layers of the pericardium. During the whole of

its retrocardiac course the esophagus lies close against the pericardium[11] and acts as a sort of sling or hammock to the heart.

Theoretical Considerations.—Wilson and his associates[68] have established the theoretical validity of the use of "semidirect" or "exploring" leads. They[69] have shown that curves obtained from an exploring electrode separated from the myocardium by media so constituted as to obey the laws governing the distribution of electrical currents in volume conductors conform to certain mathematical formulae. The soft parts of the body conduct electrical currents according to these laws. In the language of Wilson[64] (p. 613): "It is obvious that an electrode which is placed upon the heart bears no special relation to the subjacent muscle except that of nearness and that there can be no fundamental difference between placing an electrode actually upon the muscle and placing an electrode close to it, provided, of course, that in the second case the electrode is not separated from the muscle by non-conducting substance."

It has been further shown by Wilson and his collaborators[69] (p. 8) "that the potential variations produced by the heart are very large in its immediate neighborhood and diminish rapidly as the distance from it is increased, and that the potential variations of the extremities are, from a practical standpoint, negligible in comparison to those which occur within the heart itself." If the leads are so arranged in a galvanometric circuit that one electrode is close to the heart while the other is placed on the leg, the proximal electrode will be "exploring" or "different," the remote electrode will be "indifferent" and the manner of leading "semidirect." When the exploring electrode is very close to the heart, the potential changes detected by the indifferent electrode are comparatively minute and make no significant contribution to a record so obtained. In other words, the resultant curves are records of the potential variations as they affect the exploring electrode alone.

It has been established by Lewis and his associates[38] that in curves obtained from electrodes placed on the surfaces of the heart, the electrical events may be divided into two types, "intrinsic" and "extrinsic." Intrinsic deflections are those signaling the activation of the small muscle area actually in contact with the electrode. Extrinsic deflections are those resulting from electrical activity in parts of the heart muscle more or less distant from the electrode in question. The distinction is of prime importance since *a determination of the exact time relationships of intrinsic deflections establishes the time at which the explored parts of the cardiac muscle become activated.*[38] Wilson and his coworkers,[64, 68, 69, 70] have been at pains to show by carefully controlled experiments and consideration of the theoretical principles involved that under optimal conditions semidirect leads yield a faithful

representation of the electrical potential variations in the small area of muscle immediately subjacent to the exploring electrode. The essential prerequisites of an efficient or truly reliable semidirect lead therefore demand that the exploring electrode shall be very close to the heart and the indifferent electrode at a comparatively great distance from it. It has been shown that under these circumstances the intrinsic deflections maintain their true time relationships as determined by direct leads within a negligible margin of error.

As an exploring electrode is moved away from the heart, the potential variations recorded by it are quickly reduced in magnitude. The recorded curves are now correspondingly less immune to the potential variations at the site of the remote electrode. Under these conditions the lead becomes less efficient as a semidirect lead inasmuch as curves obtained by it are less faithful records of the potential variations in the previously explored small area of cardiac muscle. The intrinsic deflections are not only of smaller amplitude but also are somewhat distorted by the effect of potential variations at the remote electrode. Such distorting effects tend to disturb the true position of the intrinsic deflections to some extent. Precordial leads suffer from these disadvantages, and, when great accuracy is desirable, certain steps must be taken to exclude distortion due to the remote electrode by making it more truly "indifferent" (Wilson and his associates[67]).

In the light of these established facts it is important to reexamine the relationships of an electrode placed in the esophagus directly behind the heart. Between it and the myocardium are the esophageal wall, the connective tissue attachment, and the pericardium. The connective tissue attachment is of variable length. Near the upper pole of the auricle it is capable, post mortem, of being stretched to an extent of 1 to 2 cm., whereas below, just above the diaphragm, it may, under tension, attain a length of 3 to 4 cm. It should be possible, therefore, greatly to increase the distance between the heart and the electrode. In practice, however, fluoroscopy shows that the esophagus habitually clings closely to the posterior wall of the heart, and the electrode, when in situ, it usually discerned only as a dark object apparently imbedded in the cardiac shadow. This is particularly so when the patient is in a sitting or semireclining posture. Under these circumstances, which prevail in the procedure about to be described, the electrode is almost certainly within 1 cm. and probably within 0.5 cm. of the underlying myocardium.

From what has been stated above, it is clear that an electrode placed in the esophagus immediately adjacent to the heart is in a position to detect the variations in electrical potential occurring in that organ with advantages which cannot be duplicated by any other semidirect lead capable of easy application to the living human subject. It is

separated from the heart by a very narrow but excellent conducting barrier of tissue. Unlike precordial semidirect leads there is no interposition of poorly conducting lung tissue between it and the heart. Above all, the proximity of the esophageal electrode to the source of changes in electrical potential reduces the possible interference of the distal or indifferent electrode to negligible proportions and obviates the necessity of special measures to combat distortion attributable to that cause.

This conclusion was put to a simple test:

A dog weighing 13.2 kg. was anesthetized with dial and urethane (Ciba: 0.6 gm. per kilogram). The right auricle was exposed by a sternum-splitting operation and pericardial incision. To a point near the base of the right auricular appendix a kaolin-saline copper-sulphate electrode bearing a strand of fat-free wool (direct "nonpolarizable" electrode) was attached by a stitch. The strand of wool was insulated, except at its attached tip, by a thin rubber cover. The free ends of the thread of the affixing stitch were carried through the pericardium and then through a pad of lint 0.7 cm. in thickness saturated with normal saline solution. A silver esophageal electrode was then tied to the outer surface of the lint pad by the free ends of the original stitch thread. In this way the esophageal or semidirect electrode was superimposed upon the direct electrode and both were in a position to tap the electrical potential changes occurring in the small area of auricular muscle bearing the stitch. Each of these electrodes was attached to separate right arm terminals of a two-stringed Cambridge galvanometer, and the circuits were completed by attaching the left leg terminals to the left hind leg of the animal. By this arrangement electronegativity of the exploring electrodes was indicated by an upward deflection in the records so derived. Conventional Lead II was attached to a single-stringed Hindle galvanometer from which the light was projected by prisms to a 12 cm. camera common to all three string shadows. The circuit resistances were balanced. In this way a triple simultaneous record was obtained of an indirect Lead II, a semidirect lead with a metal esophageal electrode, and a direct nonpolarizable lead.

Figure 2 illustrates the result of this experiment. This curve has been subjected to a comparator analysis by which it was found that the onsets of the sharp upstrokes or intrinsic deflections of the auricular complexes exactly coincided in both semidirect and direct leads. The experiment, which has been successfully repeated on four different animals, is, with minor variations, a repetition of the work of Wilson and his coworkers,[68] and the results entirely confirm their views with regard to semidirect leads when the electrode is close to the heart. It has an additional interest from the point of view of the present problem in that the same type of metal semidirect electrode was used in these experiments as was used in the investigations on the human subject in the series about to be described. The same method of procedure has been followed with regard to the ventricle, to which reference will be made in the later part of this paper. In neither instance has there been any evidence of distortion of the curves as obtained by the semidirect method due to polarization effects (*vide infra*).

The Clinical Application of the Esophageal Lead

In consequence of the conclusions reached on theoretical grounds, a study of 142 human subjects by the esophageal lead was undertaken. The subjects fell into the following groups:

Normal control series	15
Those with cardiac disease	127*

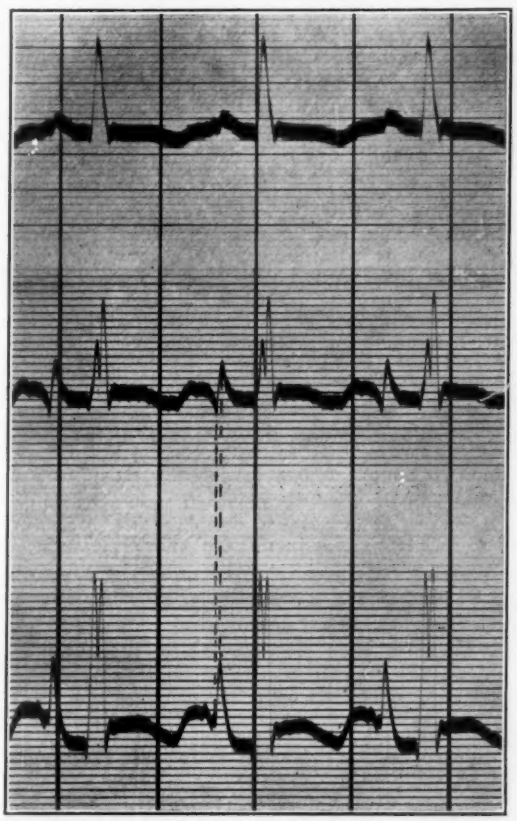

Fig. 2.—Simultaneous records from the experiment described in the text. The upper record from indirect Lead II; middle record, direct lead from the surface of the auricle; the lower record from a semidirect lead placed exactly over the area tapped by the direct lead. The intrinsic deflections are the sharp upstrokes in the auricular complexes in the two lower records. They are exactly coetaneous. The camera is at double speed; the time marker (vertical lines) indicating intervals of 0.2 sec.

Standardization of Lead II, 1 mv. = 10 mm. In the direct and indirect leads the standardization was unfortunately not recorded but is about one-third and one-half of normal sensitivity, respectively.

*The 127 abnormal cases have been classified in accordance with their outstanding cardiac manifestations as follows:

	Complete heart-block	5	
Discussed	Auricular extrasystoles	7	
in Part I.	Bundle-branch block	14	
	Ventricular extrasystoles	9	
	Second degree heart-block		3
	Aortic insufficiency (syphilitic)		2
	Hypertensive heart disease		28
Discussed	Myxedema		4
in Part II.	Rheumatic heart disease		24
	Auricular tachycardia		4
	Auricular flutter		4
	Auricular fibrillation		21
	Miscellaneous		2

The Method.—With the subject in a sitting or semireclining position the pharynx is sprayed with 5 per cent butyn solution. During this procedure the subject is instructed to inhale deeply two or three times and then to swallow. From three to five minutes later a subjective numbness or "wooden" sensation in the lower pharynx is indicative of an adequate degree of local anesthesia. The electrode is then passed in the usual manner.

Description of the Electrode.—The electrode consists of a small pear-shaped solid silver or German silver mass attached to a partially annealed German silver wire which is in turn covered by a thin soft rubber tube.

The following are the dimensions which were found to produce the most satisfactory electrode:

*The pear-shaped silver mass:**

Length (including flange)—$\frac{3}{8}$ in.
Diameter of widest part (lower end)—$\frac{5}{16}$ in.
Diameter of middle part—$\frac{3}{16}$ in.
Diameter of small flange at upper end for attachment of the insulating rubber tube—$\frac{3}{32}$ in.

The German silver wire:

Diameter—$\frac{1}{40}$ in.
Length—about 24 in.

The rubber tube:

Diameter (outside) about $\frac{3}{32}$ in. or less.
Length—20 in.

The solid silver mass is canalized in the center from apex to base to admit the wire. In the center of the base a small silver screw is made to fit into a countersunk depression. The wire is led in from the apex, and the end is securely fixed by the screw into the countersunk base. All sharp surfaces on the silver mass are carefully smoothed. The insulated rubber covering is securely tied to the apical flange and to the wire near its free projecting end. The rubber tube is marked in centimeters between the distances 25 to 45 cm. as measured from the widened lower end of the pear-shaped silver mass. The base of the truncated cone of the silver ball is downward when the electrode is introduced, thus minimizing discomfort both in swallowing and upon withdrawal.

The Technic of Passing the Electrode.—The operator stands on the right side of the patient holding the insulated wire in his right hand. The silver ball is placed on the dorsum of the tongue. The subject, in a sitting position, is instructed to hold the chin well in and to take two successive quick swallows with the teeth held apart. As this is done, the insulated wire is gently but rapidly passed through the fingers so that the electrode slips in the course of a few seconds to a depth of about 20 cm. from the teeth. He is then told to take three or four deep breaths by mouth and again to swallow. In this way the electrode in less than ten seconds reaches a depth of about 30 cm. and lies below the level of the bifurcation of the trachea, thus obviating any tendency to cough. A few deep breaths at any juncture will abolish "gagging" after the larynx has been passed.

There is no need for haste in subsequent steps. The effect of butyn is dissipated in some fifteen to twenty minutes, but in this series no undue discomfort was encountered when, in some of the experimental procedures, the electrode was retained in situ for as long as one hour.

*In a new electrode of the same dimensions all except a narrow band of the widest portion is insulated. Full tests of this electrode have not yet been completed, but polarization effects are considerably increased.

Fluoroscopic Control of the Position of the Electrode.—In ambulatory patients the next step is to determine the relationships existing between the depth of the esophageal electrode and the cardiac chambers. By using orthodiascopic technic throughout, the positions of the electrode are marked on a line drawing of the heart in terms of depth in centimeters from the teeth. It is best to begin with the electrode in position just above the diaphragm behind the base of the left ventricle. This particular position is easiest determined with the patient in the left anterior oblique position. The patient is then placed in the right anterior oblique position, and the electrode is pulled up a few centimeters at a time in successive stages and held in position by pressure of the teeth while the determinations are made. In this manner the depth of the electrode is known for each position, and the electrode can subsequently be replaced at the several points without resort to the fluoroscope.

Determination of the Position of the Electrode When Fluoroscopic Control Is Impossible.—As 22 of the series of 142 subjects were not well enough to undergo fluoroscopic examination, an additional measurement was made in all cases of the series in an attempt to acquire some other guide to the position of the electrode. With the patient in the sitting posture and the angle of the jaw horizontal, the distance from the tip of the thyroid cartilage to the top of the ensiform cartilage was measured. A comparison was made between these measurements and the depth reading on the graduated esophageal electrode and the known positions of the electrode with respect to the heart. Averaging the results in which fluoroscopic control was available, it was found that multiplication of the measurements in centimeters (tip of thyroid cartilage to the midriff) by the factor of 1.33 always indicated the depth in centimeters requisite to bring the electrode behind the left auricle. The measurement thus obtained seemed to be of more value, in that it was less arbitrary, than that of Minkowski[44] (35 to 37 cm. from the teeth).

The Galvanometer Leads and Method of Recording.—After an exhaustive comparison of all possible combinations of the esophageal lead with indifferent points, including the front and back of the chest as well as the conventional sites, it has been decided as a routine procedure to use an axial lead roughly comparable to standard Lead II. The right arm terminal of the galvanometer is attached to the projecting free end of the wire from the esophageal electrode and the left leg terminal to the left leg. *Curves taken in this manner indicate electronegativity of the right arm terminal by an upward stroke on the record.*

The electrode is placed in the position found by fluoroscopy to be just above the diaphragm and behind the left ventricle. The patient is instructed to swallow with the teeth clenched to ensure that the electrode has passed to its full depth. Successive records are then taken. Between each record the electrode is pulled up 1 or 2 cm. and held in position by the teeth. By proceeding in this manner, the whole of the posterior and postero-inferior surfaces of the heart may be

traversed in the esophageal plane until the electrode passes above the upper limits of auricular tissue. In this series six or more such records have been taken as routine, but three are usually sufficient for most purposes. Immediately after or before these records are taken, the conventional Leads I, II, and III are obtained for comparison.

At the conclusion of the operation the esophageal electrode is withdrawn by swift but gentle traction, washed, sterilized and placed in a graduate of distilled water until further use.

Comment on Detail

Difficulty With the Compensating Resistance.—In many of the newer galvanometers insufficient adjustable compensating resistance is included in the control box. It is manifest that greater compensation may be required under the conditions of procedure (one electrode internal and the other on the skin surface) than with conventional leads. When it is found impossible, as sometimes is the case, to bring the string back in front of the camera with the lead circuit fully thrown in, two adjustments may be made. The first is to reapply carefully the skin or indifferent electrode. The second is to readjust the standardization of the compensating current so as to permit a deviation of 15 degrees instead of the usual 10. This maneuver gives a 50 per cent increase of the available E.M.F. in the compensating circuit but, of course, necessitates a revaluation on that basis for each millivolt step in the adjusting resistance in the control box. The difficulty never arises in the older instruments in which a sufficient range of adjustable compensating resistance is available.

Polarization of the Electrode.—All electrodes used in electrocardiography are subject in some degree to polarization, and this is particularly intensive when small metal electrodes are used.[48] Because unduly large degrees of polarization cause serious distortion of electrocardiographic records,[31] it is necessary to examine the esophageal electrode from this point of view.

Before the above described method was adopted, repeated tests for polarization of the esophageal electrodes were made according to the procedure followed by Pardee.[48] One end of a bandage saturated with normal saline was arranged to enwrap the esophageal electrode, and the other was placed against the contact face of a German silver leg electrode 5.5 cm. by 3 cm. in dimensions. The two electrodes were then connected with a Hindle galvanometer and successive one millivolt additions or subtractions of the compensating current were made. The string was loosened sufficiently to obtain a 1 cm. deflection for each millivolt in the presence of about 2000 ohms resistance in the testing circuit.

Figure 3 illustrates the results of four such tests. Record 3 *a* shows the deflection of the string when a resistance of 2000 ohms was substituted for the testing or electrode circuit. It is to be observed that the string has been purposely left loose to obtain the full effect of polarization in the subsequent records 3 *b* and 3 *c*. Record 3 *b* is a record of standardization curves with the esophageal and leg elec-

trodes in the galvanometer circuit. The curves of record 3 *c* show the degree of polarization obtained when a second leg electrode is substituted for the esophageal electrode. Record 3 *d* illustrates the effect of adding sufficient hydrochloric acid to the saline to bring the acid concentration to about 0.3 per cent. The circuit in this instance is arranged as in 3 *b* (esophageal and leg electrodes) but the string has been made less sensitive, and this somewhat masks the increase of polarization which occurred.

In the clinical use of the method a higher degree of polarization than is illustrated in record 3 *b* has not often been encountered. Occasionally in the lower positions of the esophageal electrode a marked drifting of the string in one direction and a considerable disturbance of the standardization curve have been observed. It is possible that these

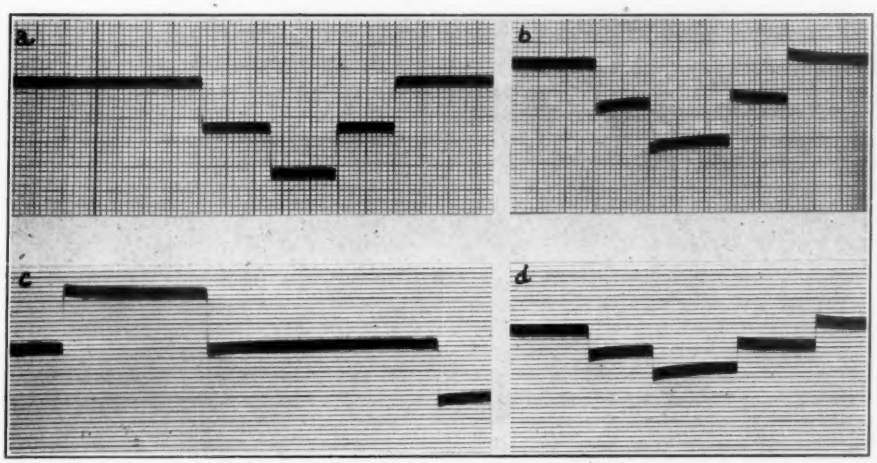

Fig. 3.—For details see text. Records *a*, *b*, and *c* are taken with the galvanometric string standardized so that 1 mv. = 9 mm. in the presence of 2000 ohms resistance. Record *d* is taken with the string sensitivity reduced to one-half this amount.

are due to regurgitation of acid stomach contents into the lower esophagus. After a few seconds the drift of the string becomes negligible although distortion of the standardization curves still, of course, remains. It is possible even in these circumstances to obtain fairly presentable curves, but there can be no doubt that they are considerably distorted.

The way in which such curves are modified by polarization requires some comment. There is interference both with the recorded amplitude and to a slighter extent with the time relationships of the more rapid changes of potential and, in particular, the returning stroke from any sharply developed peak. The above observations have been directed only to the instances in which an unduly large polarization effect is noted, and it should be emphasized that such instances are comparatively rare. Since, however, the method is subject to this disadvantage

in some degree, it is likely that detailed comparisons from case to case with respect to amplitude may lead to fallacious conclusions. On the other hand, comparisons based on the time relationships of particular deflections in the same record or in different records from the same patient are valid unless there is clear evidence of a gross change in the degree of polarization.

A large group of patients have been examined at repeated intervals, and in these comparator analyses of the curves obtained from the same esophageal sites in the same individual have shown a high degree of fidelity even to the minute details of the compared records. This is considered to be substantial evidence that the slight degree of polarization illustrated in Fig. 3 is not of a grave character. In an earlier part of this paper (Fig. 2) experimental evidence has been offered in further support of this contention. For these reasons it has been concluded that, although admittedly not entirely free from polarization effects, the electrode and the method as described may legitimately be applied to electrocardiographic investigation in the living human subject.

Phasic Deviations of Extraneous Origin.—In some patients, especially with low lying positions of the electrode, marked phasic deviations of the base line may occur. These may be very great if the electrode is in the sphincterlike diaphragmatic opening. In other positions they are chiefly due to respiratory interference. It is advisable, therefore, to have the patient arrest his breathing for the requisite time during the actual recording. Swallowing or coughing will also affect the curves.

String Standardization.—Except when otherwise stated, in all the records reproduced in this paper the string standardization is the same in the esophageal and conventional lead (1 mv. equals 1 cm.). It is expedient to restandardize the string for each new position of the electrode.

Contraindications to the Use of the Method.—Apart from patients with actual disease of the pharynx or esophagus (tumors, diverticulae, infection, abscesses, etc.) and patients who are critically ill or are vomiting, there are no contraindications to the method. Butyn is bitter to the taste; so it may be taken as a guide that if a patient who is ill cannot tolerate the mere spraying of the throat, it is useless to attempt to proceed. It should, however, be emphasized that the passage and retention of the electrode, as outlined above, occasions less discomfort and is better borne than similar procedures with duodenal or small stomach sampling tubes.

In the entire series no prolonged attempt was made to introduce the electrode. On only two occasions was the initial attempt unsuccess-

ful; both were in psychoneurotic patients. In all other instances the electrode was successfully and easily passed in less than fifteen seconds.

Summary of Section 1

1. The anatomical relations of the esophagus to the heart chambers are indicated.

2. An electrode in the esophagus behind the heart is an "exploring" or "semidirect" electrode. The theoretical considerations relating to the use of an esophageal electrode as a semidirect lead in clinical electrocardiography are reviewed, and experimental evidence is offered in support of the conclusions reached.

3. The method is described in detail and the clinical cases to which it has been applied are enumerated.

4. Certain difficulties, including polarization of the electrode, are discussed.

5. The conclusion is reached that on both theoretical and practical grounds the method may legitimately be applied to electrocardiographic studies of healthy and diseased conditions in the living human subject.

SECTION 2. AN ANALYSIS OF THE NORMAL ESOPHAGEAL CURVES FROM THE HUMAN AURICLE

In Section 1 of this paper evidence has been offered to prove that records obtained by the use of an esophageal electrode may be considered to be essentially the same as those obtained by a direct lead. For this reason it is proper to refer to esophageal curves as "electrograms" as distinct from "electrocardiograms" as obtained by indirect leads. The distinction is made in the interests of clarity, for it is obvious that a curve obtained by the esophageal method is not primarily a record of the currents of action of the heart as a whole since the heart does not lie between the two derivative electrodes. Such a curve is rather a record in which all cycles of activity of the heart are indicated but in which disproportionately great emphasis is placed on the changes of potential in one small region of cardiac muscle lying immediately adjacent to the exploring electrode.

Before proceeding to a consideration of the findings in disease, it is desirable to determine the character of esophageal electrograms in the normal human subject. To this end fifteen normal controls were examined by the method. The ages of the members of this group ranged from twenty-two to fifty-eight years. The findings obtained when the exploring electrode was lying close to the auricle will first be reviewed.

The Auricular Complex.—Figure 4 A recalls the general relationships of the esophageal electrode to the human auricle. The drawing represents the posterior surface of the heart. The esophagus is shown

overlying the left auricle and the base of the left ventricle. It is seen that normally the esophagus does not come into contact with the right auricle nor the venae cavae although it is quite possible that rotation of the heart and possibly enlargement of the right auricle may bring these structures into a closer relationship. The upper and lower limits of the left auricle are indicated by broken lines.

In Fig. 4 B, the curves *A* to *H* are those obtained from the correspondingly lettered positions of the electrode indicated in the drawing (Fig. 4 A). In positions *C* to *G*, inclusive, the electrode lies behind the

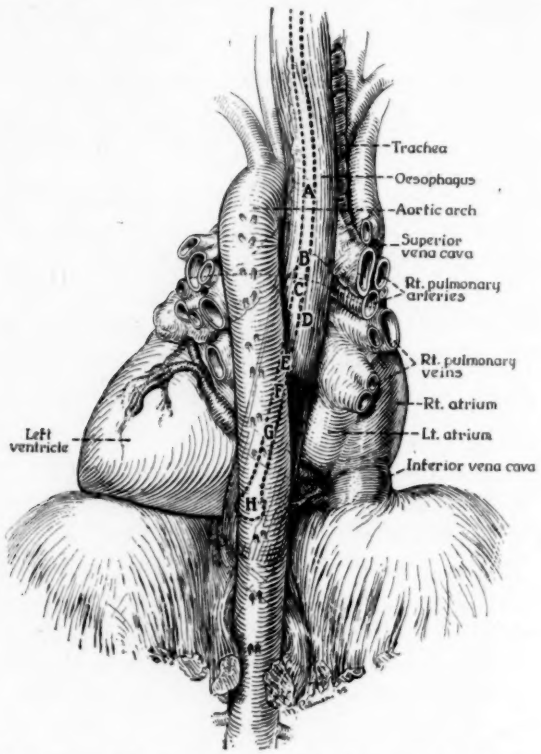

Fig. 4A.—Drawing of a posterior surface of the human heart to illustrate the position of the esophagus in relation to the left auricle and the left ventricle. The lettered areas indicate the regions tapped by the electrode. See Figure 4B.

left auricle. In these curves the P-waves have a polyphasic character. If they are examined more closely, it is apparent that they exhibit differences, the most pronounced of which concern the main upward stroke. In curve *D* this stroke occurs very early in the complex, whereas in *G* it occurs much later. It is also noteworthy that the P-waves of records *A* and *B*, obtained from positions above the level of auricular tissue, are of very different character from those just mentioned, and that *A* is very like the conventional Lead II. These curves (*A* and *B*) differ from the others (*C* to *G*) in the complete absence of any sharp upstroke.

The sharp upstroke is, therefore, obtained only when the electrode is very near auricular tissue. As already stated, such upstrokes indicate electronegativity of the small region of myocardium immediately subjacent to the electrode.

In the experiment which provided the data for Fig. 5, a double esophageal electrode was used. The principles of construction were the same as those described above except that a hole was bored in the center of the upper silver ball to permit the passage of the insulated

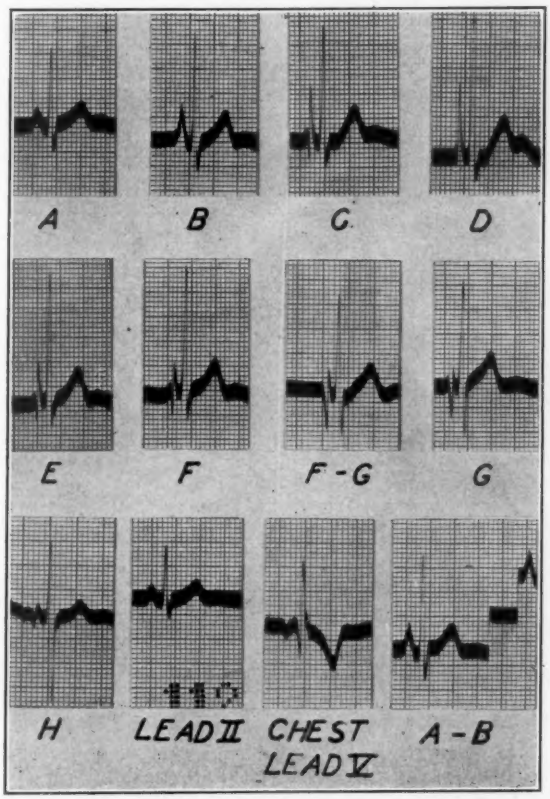

Fig. 4B.—Subject, a normal student, aged twenty-three years, illustrating the esophageal electrograms obtained respectively from the areas indicated by letters in Fig. 4A. Lead II and chest Lead V are included for comparison. Standardization for all curves is shown in record *A-B* which also demonstrates that polarization is a negligible factor. For full discussion see text.

NOTE.—The heavy vertical lines in the curves mark the time in 0.2 sec. intervals. This is true of all illustrations in the paper. In many instances as in the curves here reproduced a further subdivision into time intervals of 0.04 sec., has been made.

wire from the lower electrode. The distance between the electrodes was 4 cm. Each esophageal electrode was attached to one of the right arm terminals of a two-stringed galvanometer. The left leg served as the site of the remote electrode or indifferent lead in both circuits. Simultaneous records could thus be taken from two different points on the auricles.

The line drawing of the heart in the right anterior oblique position indicates the relationship of the two electrodes to the left auricle (crosshatched) as determined by fluoroscopy.* The records taken simultaneously from these two points are shown immediately adjacent to the drawing (curves marked *A* were obtained from electrode 1 and curves marked *B* from electrode 2). Each of these curves is also shown taken simultaneously with Lead II, care being taken to avoid any

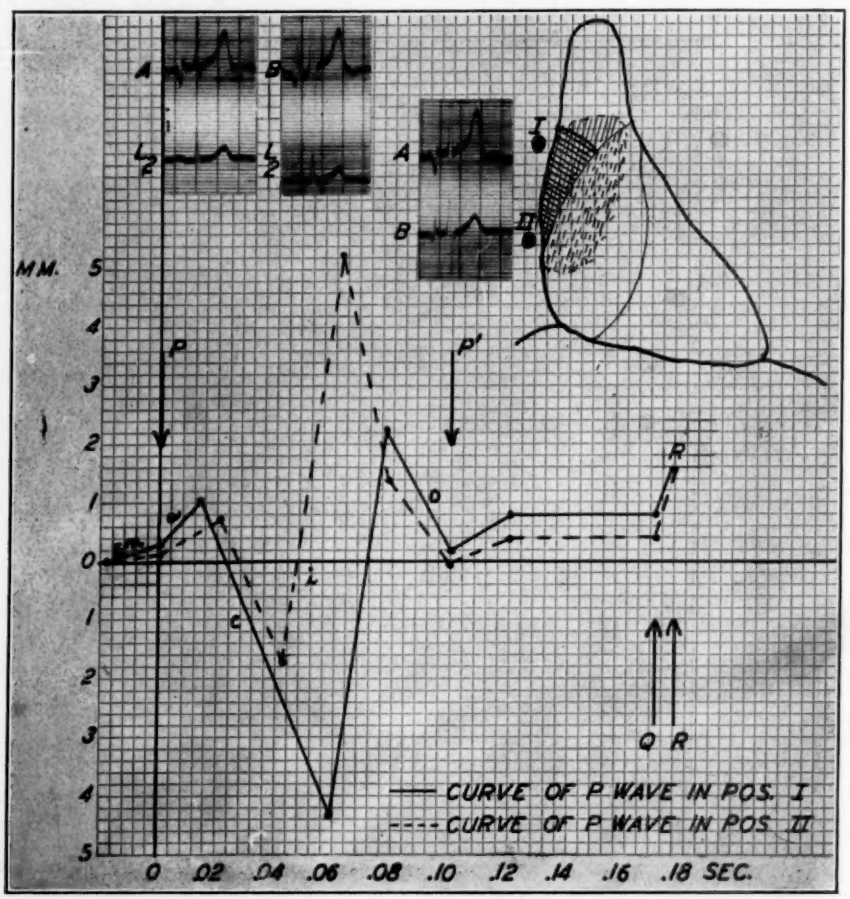

Fig. 5.—Simultaneous records from a normal subject aged fifty-two years, with graphs to illustrate the comparator findings. A double esophageal electrode was used.

The arrows at *P* and *P'*, respectively, indicate the beginning and end of the P-wave in Lead II. For a full description see text.

change in the positions of the electrodes. The accompanying graphs are based on data obtained by careful comparator analysis of the auricular curves (Lucas comparator). The P-wave of Lead II is not drawn in full but is represented as beginning at the arrow *P* and end-

*The subject was a man, aged fifty-two years, whose heart lay transversely on an unusually high diaphragm.

ing at the arrow *P'*. Each of the esophageal P-waves is shown plotted against that of Lead II and against one another.*

An analysis of the graphs shows that in each a wave *Sn* representing a very small negative potential difference starts about 0.018 sec. before the onset of the P-wave in Lead II. This is followed by a larger sluggish upward or negative deflection *a*, and this in turn by a more sharply delineated downward or positive stroke *e*. Then occurs a rapid change to negativity and the sharp upstroke *i* is written. Finally a more leisurely deflection *o* seeks the isoelectric line and ends near it simultaneously with the end of the P-wave of Lead II (arrow at *P'*).

Discussion of Interpretation.—The following explanation of these events is offered.

The low voltage wave *Sn*, which is not included in the P-wave of conventional Lead II, must represent the earliest electrical activity in the auricle. It may be that it is produced by the activation of the sino-auricular node. In this series it is frequently not discernible under the comparator for every position of the electrode, but when observed its duration is fairly constant. The range is from 0.011 to 0.018 sec., with an average of 0.0142 sec.

Wedd and Stroud[61] demonstrated in dogs with direct leads taken simultaneously with Lead II that the low grade electrical potential difference representing the activation of the sino-auricular node and the immediately adjacent structures were not included in the P-wave of conventional Lead II. They found that this wave usually started about 0.01 sec. before the onset of the P-wave. Eyster and Meek[20] confirmed this observation.

The wave which is designated *a* is thought to represent the summation of activation effects of parts of the auricle distant from the electrode. The alternative possibility that it may be due to interference from the indifferent electrode is not yet wholly to be excluded. To this end comparative records have been taken using Wilson's technic[67] for increasing the indifference of the remote electrode without significant diminution in the amplitude of the wave. The proposition that the wave *a* is wholly to be attributed to distortion from potential differences under the indifferent electrode is clearly untenable, for the occurrence of the *Sn* wave cannot be explained on this hypothesis.

The positive deflection *c* heralds the approach of the wave of excitation nearer and nearer to the cardiac tissue lying closest to the electrode. The work of Craib[9] indicates that this tissue, immediately before it becomes activated, is electropositive to the tissues which are undergoing activation in its immediate vicinity. If this interpretation

*Corrections were made for differences in standardization in the esophageal curves to permit of accurate comparison.

is correct, then all of these effects (deflections *Sn*, *a* and *e*) are "extrinsic" by the definition of Lewis.[32] They are the effects produced by activation of more and less remote portions of the auricular myocardium.

The sudden change from positivity to negativity (at the junction of deflection *e* and *i*) signals the arrival of the excitation wave at the cardiac tissue underlying the electrode. The negative deflection *i*, therefore, represents the phase of activation of this small region and is, consequently, "intrinsic" in character (Lewis[32]). In the language of Craib,[9] deflection *i* represents the passage of the activating train of doublets under the electrode; and the deflection *o* seeks the isoelectric line as the spread of excitation reaches the last unactivated portions of the auricle and dies away. The fact that deflection *o* seldom ends on the isoelectric line (but usually above or below it) and that the remainder of the P-R interval is likewise seldom truly isoelectric is in all likelihood due to the doublets of retreat or "repolarization."[9, 68, 69] This is a phase which will be more clearly demonstrated in a later consideration of the Ta-wave.

The graphical representation of curves *A* and *B* in Fig. 5 clearly indicates that the intrinsic deflections occur at different intervals in the P-wave, although their actual duration is fairly constant. The position of the *i* or intrinsic deflection in the auricular complex must, since it indicates activation of the tissue immediately underlying the electrode, be due to two factors. It must depend upon the distance separating that tissue from the origin of the wave of excitation (i.e., the length of the pathway traversed by the excitation wave) and upon the rate of conduction in the intervening auricular musculature. In the same way the position of the intrinsic deflection with respect to the isoelectric line (whether it starts below or ends above it) also depends on these factors. If the electrode becomes negative very late in the P-wave, the foregoing extrinsic effects are greater and the intrinsic deflection starts far below the isoelectric line; it may even end on it if the tissue over which the electrode lies is among the last of the parts to be activated.[68, 69] In these instances the occurrence of the *i* deflection may often be later than the summit of the P-wave in Lead II. The converse is also true. If it were possible to place the electrode exactly over the sino-auricular node, the intrinsic deflection would occur at the very beginning of P.[38] It would start from the isoelectric line and run above it. The extrinsic parts of the curve in this instance would be wholly written by the wave *o* (see Fig. 12, in which an extrasystole arose almost exactly under the electrode; also compare curve *D* with *G* in Fig. 4 B). Records obtained when the esophageal electrode is below the level of the lower pole of the auricle usually show a rather ill-defined or polyphasic P-wave of low ampli-

tude (*H*, Fig. 4 B). It is possible that such potential changes are in part due to electrical events occurring in the neighboring inferior vena cava.

The P-wave of conventional leads is thus to be regarded as the sum of numerous intrinsic electrical events of the type which has been described. This fact now demonstrated in the living human heart conforms with the experimental work of Boden and Neukirch[6] on the isolated human heart, of Wilson and others[69] on animals, as well as with the views expressed by Lewis.[32]

Recapitulation of Section 2.—When an electrode is placed in the human esophagus behind the left auricle, the recorded auricular complexes have a characteristic appearance so long as the electrode retains its close relations with the auricle. Such curves may be designated as "esophageal electrograms." When the electrode is placed at a higher level, the recorded curves take on the character of indirect axial leads not unlike those of conventional Lead II. In auricular esophageal electrograms the outstanding features of the P-wave are its polyphasic form and the presence of an intrinsic deflection. The intrinsic deflections have been accepted, on the basis of evidence offered in Section 1, as accurate indications of the time of activation of the various auricular regions explored by the esophageal electrode. Analysis of the P-waves has further demonstrated that in some cases a small wave occurs before the onset of the P-wave of conventional Lead II. This has been attributed to the influence of electromotive changes incidental to the activation of the sino-auricular node.

SECTION 3. OBSERVATIONS ON THE TA-WAVE AND AURICULAR EXTRASYSTOLES

That the P-wave of the standard electrocardiogram does not represent the electromotive changes of the auricle in their entirety has long been common knowledge. Although several observers (Kraus and Nicolai,[28] Samojloff,[55] Straub[59]) had previously described an "after-wave" which followed the P-wave of auricular contraction, Hering[24] was the first to prove that it was a part of the auricular complex. He named it the Ta-wave and considered it to be the auricular analogue of the T-wave of the ventricle. This work was confirmed in isolated heart preparations from various animals by the following workers: Hering,[23] 1909, frog; Eiger,[13, 14] 1911, 1913, frog; Noyons,[46] 1910-11, frog, carp; Samojloff,[56] 1910, cat; Kahn,[25, 26] 1909, 1911, dog; Mines,[43] 1912, frog; Bakker,[3] 1912, eel; Fredericq,[22] 1912, isolated strips of cardiac muscle of the dog; Nörr,[45] 1913, horse; Wiedemann,[63] 1917, dog; Rümke,[54] 1918, isolated strips of cardiac tissue from frogs; Boden and Neukirch,[6] 1918, and Boden,[5] 1921, the human heart.

A considerable range in duration of the Ta-wave was reported. Measured from the onset of P to the end of the Ta-wave (P + Ta interval) the following variations were noted: Eiger[14] (see curves 5, 6, 7, 11, 12, 12a of his paper) 0.25 to 0.8 sec.; Hering[24] (isolated frog's heart) 0.25 to 1.0 sec.; Eyster and Meek[20] (tortoise heart) 0.48 sec. (average); and Boden and Neukirch[6] isolated human heart 0.4 to 0.52 sec. No doubt the wide range found by the above authors was in part due to experimental conditions such as fatigue and temperature, but Boden[5] and Eyster and Meek[20] showed that other factors may change the P + Ta interval. The latter showed that in the tortoise vagal stimulation shortened the P + Ta interval and changed the form of the Ta-wave, and Boden[5] demonstrated a shortening of the P + Ta interval with acceleration of the heart rate. In a paper by Andrus and Padget,* which has not yet been published, there is evidence that the P + Ta interval is shortened with shortening of the refractory period of the auricle.

Studies of the Ta-wave in the human subject in the past were confined to data obtained from conventional leads. Sprague and White[58] published observations on the Ta-wave in a series of thirty-seven patients with complete heart-block. In eighteen cases the wave was visible in one or more leads. These waves very seldom attained a height of 2 mm. and were opposite in direction to the P-wave. Caliper measurements of the curves showed a P + Ta interval ranging from 0.34 to 0.42 sec. (average 0.37 sec.). In other words the ratio $\frac{\text{P + Ta interval}}{\text{Duration of P}}$ was about 3.7.

It has long been known that the myocardiogram of the ventricle bears a close relationship to the Q-T interval. It has also been a common observation that the auricular myocardiogram greatly exceeds the duration of the P-wave. An excellent illustration of this fact is shown in Fig. 8, p. 148 of the paper by Lewis, Feil and Stroud.[37] Caliper measurements of this figure show that the contractile phase of the auricle occupies 0.115 sec. and the total length of the myocardiogram 0.326 sec. This clearly shows that the auricular myocardiogram in the dog extends well into the ventricular complex under the conditions of normal rhythm.

That a parallelism exists between the auricular myocardiogram and the P + Ta interval is well shown in the monograph of Wenckebach and Winterberg[62] (Fig. 17, Tafel 9). The exact degree of correspondence between these values has been a subject of dispute[16, 12, 42, 2] but the interest in the Ta-wave largely arises from the relationship existing between the P + Ta interval (as indicating the total duration of the electrical events in the auricle), the auricular myocardiogram, and the length of the refractory period of auricular muscle.

*Personal communication.

In the present series careful comparator studies were made of the P + Ta interval whenever opportunity presented. Several good examples of such waves were found. As would be expected, they were

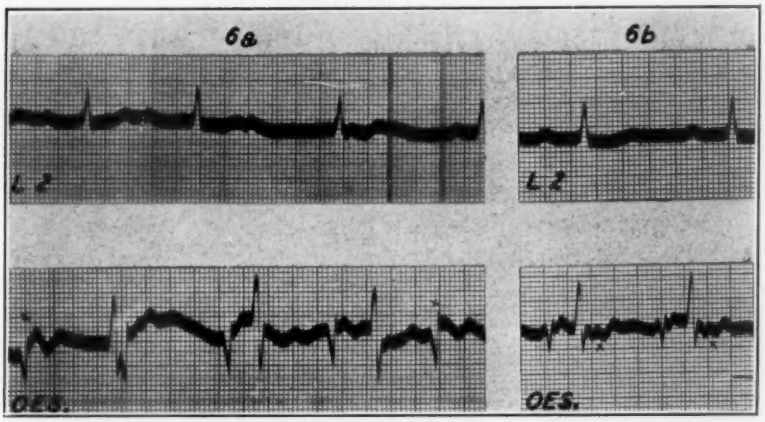

Fig. 6.—Patient B. M. The curves on the left (6*a*) show conventional Lead II (upper curve) and an example of an esophageal electrogram in a patient with complete auriculoventricular dissociation. The complexes marked with a cross are followed by Ta-waves. On the right (6*b*) are similar curves obtained with reduced string sensitivity from the same patient under conditions of first degree heart-block. The crosses indicate a small wave described in the text.

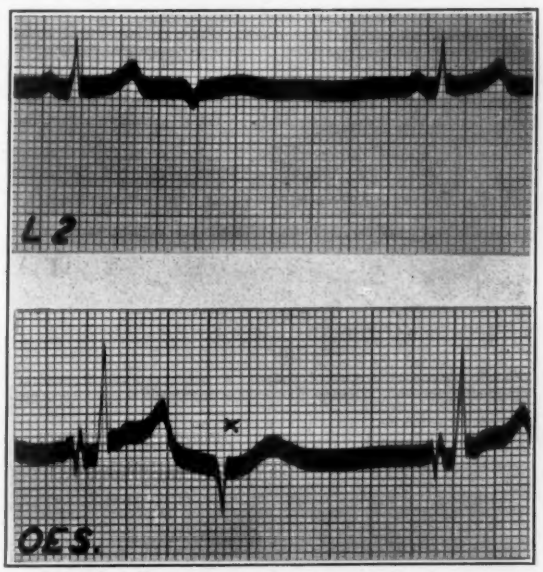

Fig. 7.—Patient B. C. Lead II above and an esophageal lead below. Complex marked by cross shows an ectopic auricular extrasystole followed by a Ta-wave. (See also Table I.)

of much greater amplitude and more clearly shown than in any previously published examples from the living human subject.

Figures 7 and 8 illustrate records from women in whom frequent auricular extrasystoles were occurring from ectopic foci. These are

not followed by ventricular contractions and the Ta-waves are clearly discernible both in the esophageal curves and in Lead II.

Figure 6 *a* shows records taken from a male subject forty-five years of age who suffered from Adams-Stokes attacks. A complete auriculo-ventricular dissociation is present (cf. also Fig. 9). At the points

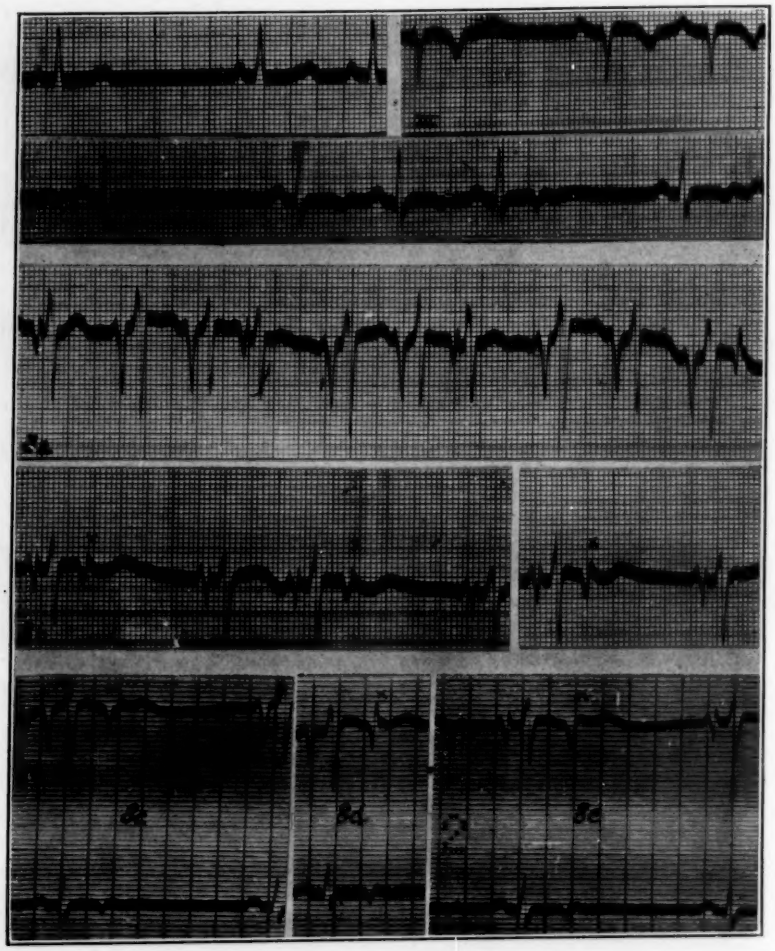

Fig. 8.—Patient A. J. (See Table I.) Records obtained from a patient showing numerous auricular extrasystoles. Conventional Leads I, III and II, are at the top. Records *8a* and *8b*, are esophageal curves from two different auricular sites. The crosses indicate auricular complexes followed by Ta-waves. Records *8c*, *8d*, and *8e* show simultaneous records obtained one month later. Lead II is shown below, and curves from the esophageal electrode at various levels are shown above. Note the frequent occurrence of Ta-waves and the form of the ectopic P-waves as contrasted with those arising in the usual site.

marked with crosses the auricular complexes occur at the end of the T-wave of the preceding ventricular complex. Such P-waves are followed by a clearly defined biphasic wave, the Ta-wave. Figure 6 *b* shows records from the same man on the next day when sequential rhythm with a first degree heart-block was present. In the esophageal

records of this example a tiny wave interrupts the ventricular S-T interval. It is found, on measurement, that the distance from the beginning of the P-wave to the end of this wave is almost exactly equal to the P + Ta interval in Fig. 6 *a*. The record also suggests that, if a first degree heart-block were not present, this wave would fall near the onset or even on the ascending limb of the ventricular T-wave of esophageal electrograms. The comparator measurements obtained from the examples encountered in the series including those cited above are shown in Table I.

It will be seen from the measurements given in Table I, that the duration of the P + Ta interval as measured from the beginning of the P-wave to the end of the Ta-wave ranges from 0.405 to 0.503 sec. and that the ratio of $\frac{P + Ta}{P}$ may be as high as 5.63 and as low as 4.05.

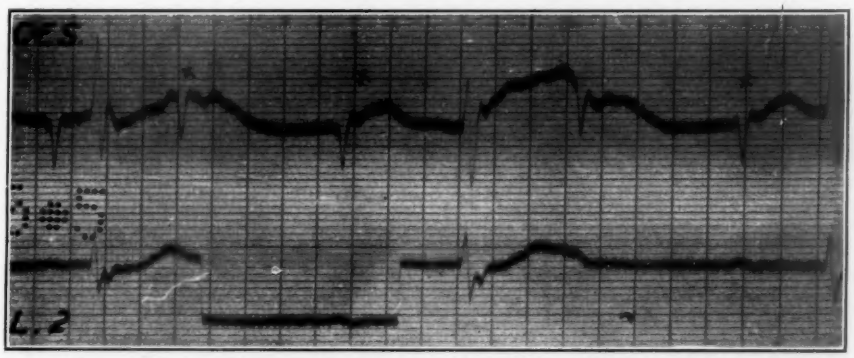

Fig. 9.—Patient H. G. Complete A-V dissociation. Upper curve, and esophageal lead. Lower curve, simultaneously written conventional Lead II. Complexes marked by a cross show Ta-waves. (See also Table I.)

The average ratio for all cases investigated is 4.72, a figure considerably greater than that found by Sprague and White.[58] This finding is of additional interest inasmuch as the duration of the P-wave as measured in esophageal electrograms is usually longer than that found in conventional leads (Fig. 5).

There is considerable variation in the character, though not the length, of the Ta-wave in the same patient, depending on the position of the esophageal electrode. The amplitude and the direction of the wave or its components are found to vary for different positions of the esophageal electrode. On occasions the after deflection is preceded by a return to the isoelectric line (Fig. 7) comparable to the S-T segment of the ventricle. In records from other esophageal sites in the same patient all trace of the isoelectric phase may disappear. Similarly a wave which is upright in one position of the esophageal lead may become biphasic in other positions. These variations are frequently to be seen affecting the P-R interval in many of the curves

TABLE I

PATIENT FIG. NO.	COMPLEX MEASURED	TYPE OF RHYTHM PRESENT	DURATION OF P-WAVE IN SECONDS	DURATION OF P + Ta INTERVAL (TOTAL AURICULAR COMPLEX) IN SECONDS	RATIO $\frac{P + Ta}{P}$	AVERAGE $\frac{P + Ta}{P}$ RATIO
B. C. 7	Normal P-wave. The auricular extrasystole	Normal sinus rhythm with occasional auricular extrasystoles	0.0910			
			0.0974	0.480	4.94	4.94
B. M. 6 *a.*	Indicated by crosses	Complete A-V dissociation	0.0988	0.5030	5.19	
			0.1001	0.5006	5.00	5.095
B. M. 6 *b.*	Same patient. Indicated by crosses	Sinus rhythm with first degree heart-block		To end of small wave in S-T segment		
			0.1029	0.5014	4.87	
			0.1006	0.4930	4.90	4.885
A. J. 8	Indicated by crosses	Multiple auricular extrasystoles	0.1180	0.512	4.34	
			0.1146	0.496	4.33	
			0.1142	0.498	4.36	4.345
G. B.		Complete A-V dissociation	0.1064	0.461	4.33	
			0.1064	0.431	4.05	4.19
H. G. 9	Indicated by crosses	Complete A-V dissociation with auricular bigeminy	0.0742	0.408	5.49	
			0.0740	0.406	5.49	
			0.0728	0.405	5.63	5.53
B. S.		Complete A-V dissociation	0.1082	0.440	4.06	
			0.1074	0.438	4.08	4.07
A. A.		Complete A-V dissociation	0.1016	0.462	4.55	
			0.1008	0.457	4.58	4.57
		Average Values	0.0992	0.464	4.72	

shown in this paper in which a high take-off of the Ta-wave causes a marked deviation of the P-R interval from the isoelectric line under conditions of sequential rhythm.

There is no doubt that the Ta-waves in esophageal curves exert some influence on the S-T segment of the ventricular curves for they certainly extend well into this part of the complex. This is well illustrated in Fig. 10. In this record there are three instances when the ventricular complex is not preceded by an auricular complex (sino-auricular block or standstill). The S-T segments of these ventricular curves are decidedly different from those modified by an antecedent auricular complex. The form of the ventricular complexes themselves does not vary, and it is justifiable to assume that they are all of supra-ventricular origin. It is too much to suggest that comparatively large

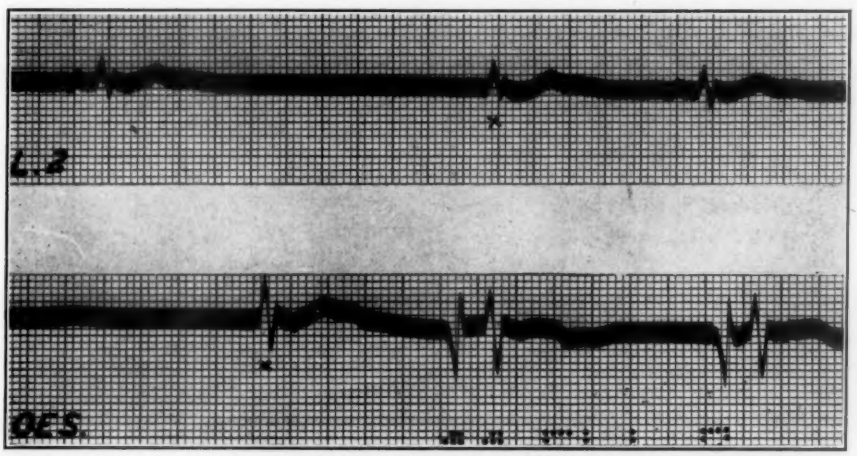

Fig. 10.—Patient W. E. Conventional Lead II above, esophageal electrogram below illustrating sino-auricular block and the modifying effect on the S-T segment by the Ta-wave. Complexes marked with a cross denote ventricular escape.

modifications of the ventricular S-T segment may be due to this cause in indirect or conventional leads. It should be noted, however, that there is great variation in the amplitude of auricular T-waves from patient to patient and that Sprague and White[58] have been able to detect definite waves in 50 per cent of their series, some being as high as 2 mm. In view of these facts it is timely to sound a warning against interpreting minor deviations of the S-T segment of conventional curves as evidence of ventricular damage, for they may be caused by auricular events which extend farther into the ventricular complex than has generally been recognized.

Auricular Extrasystoles.—Early papers by Lewis[33, 35] have placed emphasis on the variations in form of the P-waves of conventional leads as indicating the ectopic origin of auricular extrasystoles. In Figs. 7 and 8, which have been referred to before, the differences in the

form of the P-wave of the esophageal electrograms in extrasystolic and normally occurring complexes are well illustrated. In Fig. 11 an example is given of auricular extrasystoles occurring in the presence of complete A-V dissociation, the interpolated beats causing an auricular bigeminy. The differences in the form of the coupled auricular beats in these records recall the P complexes of Fig. 5. In Fig. 5

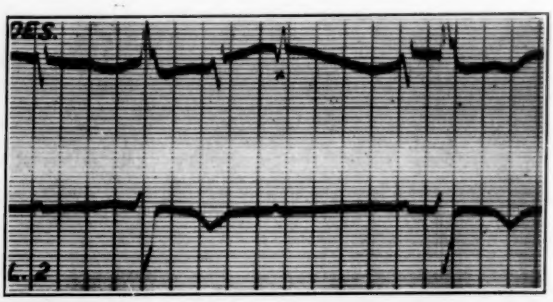

Fig. 11.—Patient G. B. A case of complete A-V dissociation and intraventricular block which illustrates auricular bigeminy at points indicated by crosses. The interpolated auricular complexes clearly arise from ectopic foci since they differ in form from the regularly occurring beats.

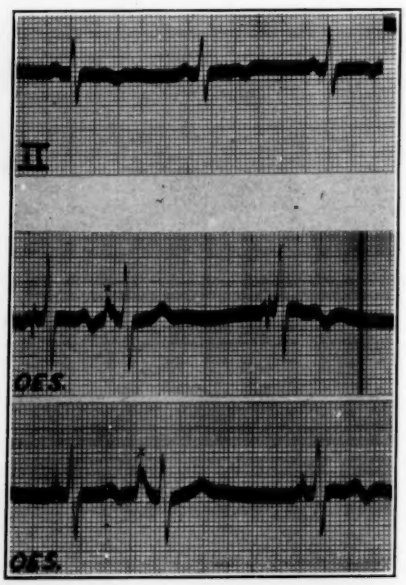

Fig. 12.—Patient D. W. Auricular extrasystoles. The lower two records are taken from esophageal leads. Lead II is shown above. The extrasystoles are indicated by crosses. The ectopic complex in the lower record arises from the region almost exactly below the electrode. Standardization, 1 mv. = 7 mm. in esophageal curves.

one focus is acting as origin for all auricular beats, and the differences in the complexes obtained from the two separate exploring electrodes are due to the fact that the electrodes were at unequal distances from the sinus node. Figure 11 presents the converse of this, for here the single electrode remained stationary, and two different foci were in effective action.

In Section 2, reference has been made to a record showing an extrasystole originating almost exactly under the esophageal electrode. This is exemplified in Fig. 12 (lower curve). The complex begins at once with an intrinsic deflection, and this is followed by a long extrinsic after effect. The total duration of the ectopic P-wave is 0.1367 sec. as compared with 0.0849 sec. for the normally occurring P-waves. The following explanation for this prolongation of the length of the P-wave appears reasonable. It is known from the experiments carried out in Lewis' laboratory[34, 39, 38] that the normal excitation wave starts from the sino-auricular node and spreads radially throughout the auricle. In the present instance the wave is known to arise at an eccentric point in the left auricle at some distance from the sinus node. To reach the furthermost tissue of the right auricle, it must therefore travel considerably farther and consume more time in transit than is normally the case.

It seems safe to predict that a more general use of the esophageal lead might soon result in criteria for the localization of auricular extrasystoles and thus supplement the early work of Lewis[35] in this field.

Recapitulation of Section 3.—Several examples of clearly visualized auricular T-waves have been illustrated, measured, and discussed. The conclusion has been reached that this part of the auricular electrical cycle may extend much farther into the S-T segment of the ventricular complex than has hitherto been recognized and cause minor deviations from the isoelectric line in conventional leads.

Examples of auricular extrasystoles have been illustrated and the suggestion has been made that a wider use of the esophageal method might be helpful in determining the position of the focus responsible for the ectopic beats.

SECTION 4. AN ANALYSIS OF THE VENTRICULAR COMPLEXES OF ESOPHAGEAL LEADS IN NORMAL INDIVIDUALS

In Fig. 4 B, in which the standardization of the string is the same in all curves including the conventional and chest leads, it is at once apparent that the whole of the ventricular complex is exaggerated when compared with Lead II. The T-wave is wider and more pointed, having its onset earlier and frequently being followed by a U-wave.

It is further to be noted that in no curve obtained with the esophageal leads in Figs. 4 B, and 5, is a Q-wave present. Comparison with Lead II in this latter figure shows that the onset of the R-wave in the esophageal lead precedes that in Lead II. Under the comparator (as is indicated in the graph) the R-wave of the esophageal curves is seen to coincide with the earliest sign of activity in Lead II. In the conventional lead this event is written as a tiny Q-wave. In all of the normal controls and in all but a very few of the abnormal cases the

earliest sign of ventricular electrical activity is always an upstroke or R-wave when the electrode is behind auricular tissue. The onset of the R-wave in such esophageal curves coincides with R of Lead II only when no trace of a Q-wave is present in that lead.

The following suggestion is offered in explanation of this fact. If an exploring electrode is placed against, or almost against, auricular musculature, then at the onset of ventricular excitation it is tapping the electropotential changes occurring in the ventricle under peculiar circumstances. It is connected to the internal surface of the ventricle by an electrolytic medium: the wall of the auricle and the auricular contents. The atrioventricular valves are open. Now it has repeatedly been shown that the earliest sign of activity in the normally beating ventricle is manifested by electronegativity of the endocardial surface. Lewis[40] and Wilson[68] have both shown, in collaboration with others, that this electrical change can be detected by an electrode placed in the blood inside the ventricular chamber. By analogy the esophageal electrode, though more remotely situated, registers initial negativity as the first sign of ventricular activity.

Apart from the above mentioned peculiarities, *the ventricular complexes obtained when the esophageal electrode is lying close to auricular musculature* closely simulated in their general character the QRS complexes of Lead II. Although this was true in all but one subject of the control series, there were frequent exceptions in the series as a whole. In such instances the ventricular complexes of the esophageal curves had a biphasic form with a well-defined S-wave. An analysis of the material of the entire series to determine the association of such biphasic esophageal complexes to ventricular preponderance gave the following results: In all cases of right ventricular preponderance the esophageal ventricular complexes were always monophasic and upright, and in all cases of left ventricular preponderance they were biphasic with deep S-waves. In the cases which fell between these two extremes, there was in general a close similarity to the QRS complexes of Lead II. In those instances in which the QRS complex of Lead II was monophasic while some of the esophageal ventricular complexes were biphasic, the position of the electrical axis in conventional leads approached in greater or less degree the border line between the normal range and left axis deviation. In these circumstances the biphasic ventricular complexes occurred in the curves obtained from the lower auricular positions of the esophageal electrode (Figs. 5 and 13). In other words, the ventricular curves showed an increased depth of the S-wave as the electrode approached the atrioventricular groove and the ventricular musculature.

When the electrode is placed below the level of the auricular musculature and close to the basal portion of the left ventricle (position *H*, Fig. 4 A), characteristic changes occur in the form of the electro-

gram. The P-waves take on the slurred ill-defined form which has already been noticed in Section 2, while the QRS complexes at once become decidedly biphasic in character, a diminished R-wave being followed by an exaggerated, deep S-wave (Fig. 13). This striking alteration in the form of the ventricular complex for juxta-ventricular positions of the esophageal electrode in normal individuals demands elucidation. Most particularly is it desirable to determine whether the appearance of the S-wave is due to the influence of an intrinsic deflection arising in the ventricular area explored.

Admittedly, an electrode in the lower esophagus does not always lie as close to the heart as it does at the auricular levels (Fig. 1), but there can be no doubt that it is, in this location, closer to the base of the left ventricle than is a precordial lead to the surface of the right ventricle. It follows, therefore, that the arguments of Wilson and his associates[68] relating to intrinsic deflections in precordial leads over the right ventricle must apply *a fortiori* to the esophageal electrode when the latter is employed as an exploring lead to the left ventricle.

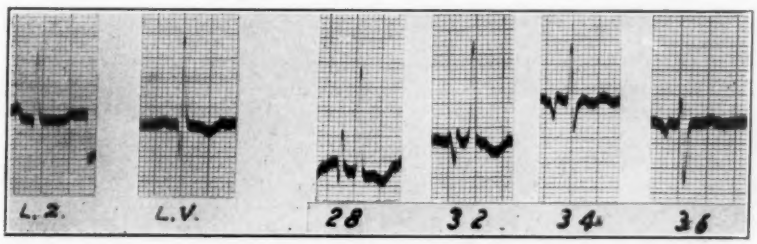

Fig. 13.—Patient L. B. Single records demonstrating the changes in the ventricular complex in esophageal electrograms for different positions of the electrode. Lead II and chest Lead V are included for comparison. The figures below the records indicate the depth of the electrode in centimeters as measured from the teeth. Note the appearance of an S-wave in the QRS complex when the electrode is near the atrioventricular groove (at 34 cm.) and the diminution of the R-wave and great increase in the amplitude of S when (at 36 cm.) the electrode reaches a juxta-ventricular position.

Lewis[32] (p. 115) has estimated on the basis of experimental findings in dogs that, in a normal human subject, the basal portion of the left ventricle may be activated as late as 0.065 sec. after the beginning of ventricular excitation. In arguing from this standpoint, it becomes obvious that a ventricular intrinsic deflection recorded by the esophageal lead must occur relatively late and, in fact, almost at the end of the QRS complex. As Lewis and Rothschild[40] have shown, the excitation wave spreads very rapidly along the Purkinje system of both ventricles, the septal portions of the musculature being first excited. The main factor responsible for the difference in time at which signs of activation appear on the epicardial surfaces of the ventricles is the relative thickness of the slowly conducting ventricular musculature of the two chambers. These facts explain why, in the normally functioning heart, the pericardial surface of the right ventricular base is

activated in advance of the corresponding portion of the left ventricle. This also explains why right ventricular preponderance tends to reverse this relationship and why preponderance of the left ventricle tends to accentuate the differences in time of activation.

It is the rule in all the normal cases studied by the esophageal electrode in juxta-ventricular positions to find that the beginning of the upstroke of the S-wave occurs progressively later as the electrode is moved upward and nearer to the free margin of the ventricular base. In the series of fifteen normal subjects the average time of onset of the upstroke in the S-wave has been found to lie between 0.04 and 0.058 sec. after the beginning of ventricular activity. In cases of left ventricular preponderance it has occurred as late as 0.063 sec. and its time of occurrence has shown an approximate relationship to the total length of the QRS complex. When marked right ventricular preponderance is present S is sometimes absent and may be represented by a notching or slurring in the downstroke of the R-wave. Because almost all esophageal records from the left ventricle of normal cases show a well-defined R-wave, it is extremely unlikely that the onset of the S-wave in the electrograms is to be taken as the exact time of onset of the intrinsic deflection arising in the muscle underlying the electrode. In other words the R-wave of such esophageal electrograms is certainly extrinsic in nature and is produced by the activation of areas of ventricular muscle at some distance from the electrode. The downstroke of the R-wave must represent the development of electropositivity in the small area tapped by the electrode. It is the resultant of extrinsic potential variations produced at a distance and charges produced in the area immediately adjacent to the electrode. The nearer the electrode is brought to the surface of the ventricle, the less is the manifest influence of the distantly arising extrinsic potential differences, and the less the influence of potential changes at the remote electrode on the left leg. For this reason curves obtained with the electrode closely opposed to the ventricle have the smallest R-waves and the largest S-waves and are those in which a determination of the time relationships of the upstroke of the S-wave most accurately represent the true position of the intrinsic deflection arising from the base of the left ventricle.

An experiment was devised to prove that the above argument is substantially valid and that the intrinsic deflection from the epicardial surface of the base of the left ventricle occurs at the approximate time occupied by the upstroke of the S-wave in esophageal leads from that part of the heart.

A dog weighing 12 kg. was anesthetized with dial and urethane. The heart was exposed by the removal of a section of the thoracic cage and splitting of the pericardium. The free end of a woolen strand was stitched to the left ventricle 1.5 cm. from the atrioventricular groove. The remainder of the strand was insulated

by rubber so that it was prevented from coming into contact with any part of the heart. The strand of wool, thoroughly moistened in saline, was fixed in a "non-polarizable" kaolin-paste copper-sulphate electrode, which in turn was attached to the right arm terminal of a two-stringed Cambridge galvanometer. The free ends of the thread stitching the electrode to the heart were then passed through the pericardium and loosely tied around the underlying esophagus at a point opposite the site of fixation. An esophageal electrode of the type used in clinical research was passed into the esophagus until the silver bulb lay opposite the ventricular area tapped by the direct lead. This electrode was attached to the right arm terminal of the second galvanometer string. Indirect Lead II was attached to a Hindle galvanometer. The left leg was used as a site for electrodes, completing each of the

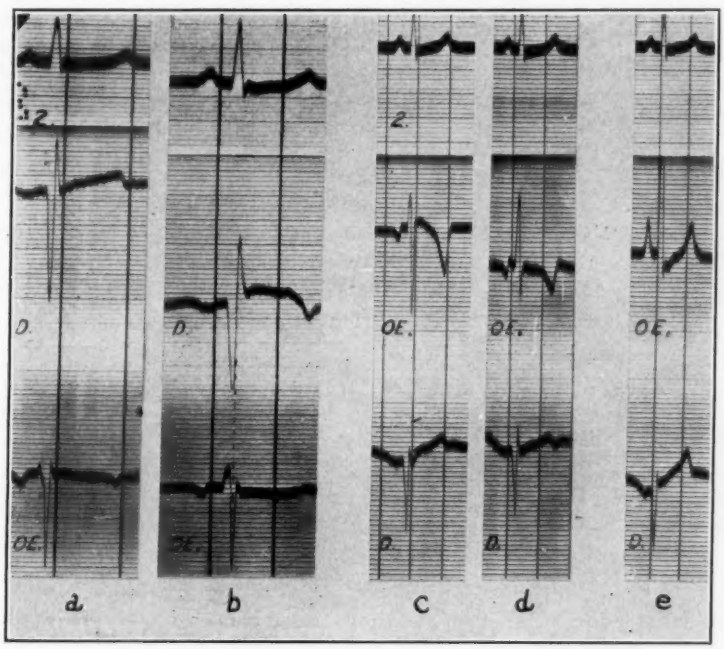

Fig. 14.—Records illustrating the findings in three animal experiments to determine the relationship existing between the S-waves of juxta-ventricular esophageal electrograms and the true intrinsic deflections as obtained by direct leads from the base of the left ventricle. The leads are recorded simultaneously; *2*, Lead II; *OE*, esophageal curves; and *D*, direct leads. For a full description see text.

three circuits. The resistances of all three circuits were balanced. By the use of appropriate prisms simultaneous tracings from the three leads were recorded on one camera.

Sample curves from three of five such experiments are shown in Fig. 14. Records *a* and *b* are taken from two different dogs. Although no R-wave is present in either of the direct electrograms (middle curves), the (lower) curves from the semidirect leads have an initial upward deflection. The onsets of the upstrokes of the S-waves are also later than the onsets of the simultaneously recorded intrinsic deflections in the direct leads, but they coincide exactly with the point at which the latter cross the isoelectric line.

Records *c*, *d*, and *e* of Fig. 14 have been obtained from a third animal. The esophageal leads in this instance are recorded in the middle and the direct leads in the lower curves. Record *c* is very similar to records *a* and *b*, but in record *d* the esophageal electrode has been displaced to a position 2 cm. away from the heart, while in record *e* the electrode has been moved to a position 2 cm. nearer the head of the animal. Both of these maneuvers have resulted in noteworthy alterations in the QRS complexes of the curves recorded by the semidirect (esophageal) lead. The R-waves in each instance have become much more prominent, and the S-waves are greatly reduced in amplitude. The upstroke of the S-wave in records *d* and *e* has also lost all pretense of representing the position of the intrinsic deflection signalling the time of activation of the base of the left ventricle. The results of these and two other similar experiments are important because they afford proof that the intrinsic deflections from the base of the left ventricle normally occur near the end of the QRS complex and that the deep S-wave of juxta-ventricular esophageal electrograms is to be attributed to the influence of such intrinsic deflections.* It is concluded that in the normally beating human heart the upstrokes of the S-waves of esophageal electrograms from the region marked *H* in Fig. 4 A, Section 2, are indicative of the approximate time at which the adjacent ventricular surface becomes activated as long as the electrode is fairly close to the ventricle. A review of the findings in fifteen normal cases indicates that abnormal delay in activation of the base of the left ventricle is demonstrated when the upstroke of a deep S-wave of a juxta-ventricular esophageal electrogram begins later than 0.065 sec. after the onset of ventricular activity. In cases of intraventricular delay it is likely that the esophageal electrogram is usually a more faithful guide to the time of activation of the left ventricular base, for, under the circumstances, there may be less interference from powerful extrinsic electrical forces arising in remote areas of the heart, these having had time to pass the zenith of their influence.

Recapitulation of Section 4.—When the esophageal electrode is lying behind auricular musculature the ventricular complexes, though somewhat exaggerated in amplitude, commonly bear a close resemblance to those of conventional Lead II. In cases of left ventricular preponderance they are usually biphasic in type, particularly when the electrode approaches the auriculoventricular junction. When the electrode is placed below the auricle in a juxta-ventricular position, not only do the P-waves become ill defined but, in the absence of marked right ventricular preponderance, the QRS complexes invariably become ex-

*The interference from extrinsic sources invariably acts to delay the onset of the upstroke of S. For this reason the onset of the true intrinsic deflection tends to precede this upstroke. It is probable, therefore, that in a normal human heart the base of the left ventricle is never activated later than 0.055 sec. after the beginning of the QRS complex.

aggeratedly biphasic. The amplitude of R decreases and S becomes disproportionately large. From both theoretical and experimental standpoints there is strong evidence that, provided the electrode is close to the base of the ventricle, the upstroke of the S-wave may be accepted as indicating the approximate position of the intrinsic deflection caused by the activation of the region adjacent to the electrode. The region so tapped by the esophageal electrode in its juxtaventricular position is the base of the left ventricle, and the position of upstroke of the S-wave of such curves may therefore warrantably be taken as a guide to the time at which the pericardial surface of that part of the heart becomes activated. Abnormal delay in activation of the base of the left ventricle is certainly indicated when in such curves a deep S-wave begins its upward stroke later than 0.065 sec. after the onset of the QRS complex.

SECTION 5. OBSERVATIONS ON CLINICAL CASES OF BUNDLE-BRANCH BLOCK AND VENTRICULAR EXTRASYSTOLES

Bundle-Branch Block.—The literature bearing on this much disputed subject has recently been reviewed by Mahaim.[41] It is sufficient for immediate purposes to indicate the present views of the opposing schools of opinion. The "old terminology," so widely accepted on the evidence offered by Kraus and Nicolai,[29] Eppinger and Rothberger,[17] Eppinger and Stoerk,[18] Lewis,[36] and Carter[7, 8] (to mention only a few), has confidently survived the early criticisms of Fahr,[21] and Oppenheimer and Pardee[47] only to bend before renewed and recent attacks. The startling results of Barker, Macleod, Alexander, and Wilson[4] from experiments on the exposed living human heart in situ have been followed by painstaking and original researches by Wilson, Macleod and Barker.[64, 68, 70, 71] The results of their investigations have led them to conclude that the interpretations of the "old terminology" are precisely the reverse of what they should be. The evidence offered in support of the "new" and now widely accepted interpretation of standard records in cases of bundle-branch block has in turn been called in question by Rothberger[50] and Mahaim.[41]

Wilson and his collaborators[68] postulate that curves showing divergence of the chief deflections in standard Leads I and III indicate left bundle-branch block; whereas these, by far the commonest type found in intraventricular delay in clinical electrocardiography, have previously been attributed to block of the right bundle. A considerable part of the evidence which has been brought in support of their conclusions is electrophysical and mathematical in character, but the data have been used as a foundation for careful research on animals and clinical cases. The approach of the Wilson school has been essentially on a functional basis in that they have largely disregarded morbid anatomical investigations and have used the electrocardiograph as an

indicator for determining the order in which the ventricles become activated. To this end they have employed precordial leads in an exploring rôle and have attempted by this means to detect delay in the activation of the affected ventricle by measuring the time of occurrence of the intrinsic deflections from both chambers. In their investigations they have had to contend with certain difficulties, not the least of which has had to do with the effective application of the exploring electrode. It is, apparently, comparatively easy to obtain trustworthy intrinsic deflections from the right ventricle by chest leads, but Wilson[68] has himself expressed dissatisfaction with some of his attempts to "tap" the left ventricle.

Rothberger[50] and Mahaim,[41] in company with a considerable number of other workers, are ranged in opposition to the views of the Wilson school and the new terminology. Both of these observers believe that the right bundle is much more commonly blocked than the left but that an interruption of conduction in the right bundle is very seldom unassociated with a partial block on the left side. Rothberger bases his conclusions on earlier experimental work with Winterberg[52, 53] which he has recently elaborated.[50] Mahaim[41] has attacked the problem by meticulous researches in the pathological field. He has subjected the whole of the previously published evidence to a strict analysis and has added much new material from his own exhaustive microscopic studies of post-mortem hearts from clinical cases of intraventricular block. While it may be stated that the majority of the electrocardiographic curves from his cases are not typical examples of the classical types described by Carter,[7, 8] a great contribution has been made by Mahaim in pointing out the comparative rarity of lesions confined to a single bundle in either ventricle. Mahaim believes that the great majority of cases of bundle-branch block are due to coronary arterial disease. He is particularly insistent that the commonest syndrome is due to a total block of the right bundle associated with block of the anterior branches of the left bundle. As an occlusive process in the anterior interventricular or septal branch of the anterior descending branch of the left coronary artery is alleged to interfere with the blood supply to these parts of the ventricular conducting system, there is cogency in his argument, and the concept of "mixed blocks" is rapidly gaining wider acceptance.[50, 52, 53, 65, 66]

As soon as it became evident that the lower esophageal lead offered an approach to the base of the left ventricle, the method was applied to the problem in hand. Fourteen cases of bundle-branch block were investigated along the following lines. The esophageal electrode was placed with the aid of fluoroscopy in a position close to the basal surface of the left ventricle (Position *H*, Fig. 4 A) below the level of the left auricle. A small German silver electrode was placed on the chest at a point 3 cm. to the left of the sternum in the fourth

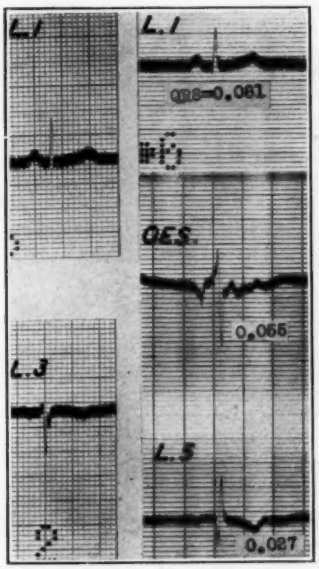

Fig. 15.—Patient G. G. From a man aged forty-eight years who showed no sign of intraventricular block. Standard Leads I and III are indicated on the left. A triple record illustrates the simultaneous recording of Lead I above, juxta-ventricular esophageal lead in the middle and Lead V below. The times of onset of the intrinsic waves in the two exploring leads are indicated by decimal fractions of a second. This example serves as a normal control for comparison with the curves of bundle-branch block.

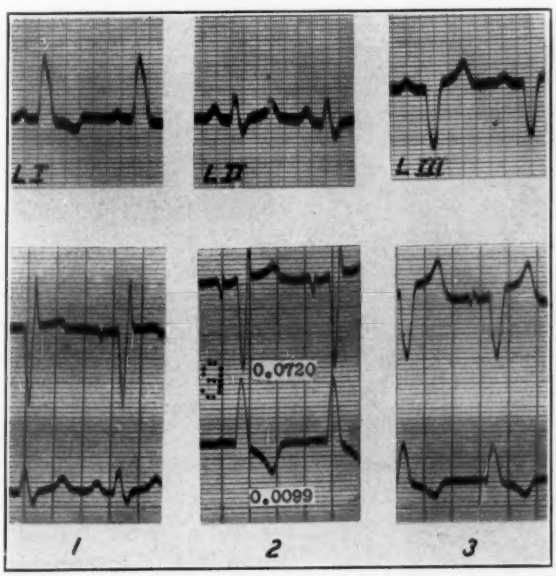

Fig. 16.—Patient M. H. Bundle-branch block of common type. Upper row: Leads I, II, and III. Lower row: *1*, esophageal electrode at 40 cm. combined with Lead II; *2*, esophageal electrode at 38 cm. combined with chest Lead V; *3*, esophageal electrode at 36 cm. combined with Lead II. The numbers below the curves in record *2* denote the time at which the respective intrinsic deflection begins.

Conclusion: An example of left bundle-branch block.

interspace. The right arm terminal of one string of a two-stringed Cambridge galvanometer was attached to each of these exploring electrodes and left leg terminals to remote or indifferent electrodes on the left leg. *Electronegativity of both the esophageal and precordial exploring electrodes under these circumstances was indicated in the curves by sharply delineated upward deflections.* The times of occurrence of such major upwardly directed deflections were determined by the comparator by measuring from the earliest sign of ventricular activity to the onset of the said deflections.

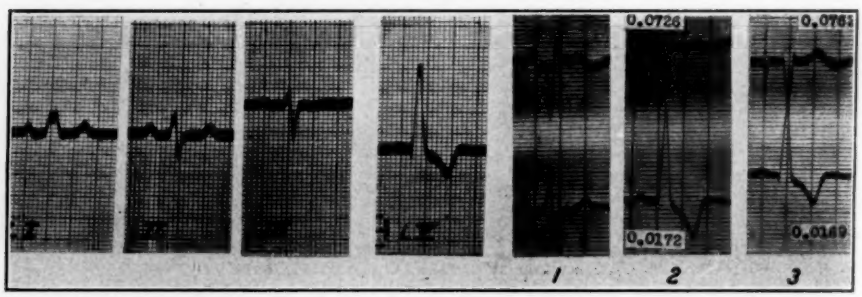

Fig. 17.—Patient A. O'L. Bundle-branch block of the common type. From left to right the single curves are Leads I, II, and III; chest Lead V. From left to right double curves (esophageal curves above): *1*, esophageal electrode at 36 cm. combined with Lead II; *2*, esophageal electrode at 36 cm. combined with chest Lead V; *3*, esophageal electrode at 34 cm. combined with chest Lead V.

The decimal fractions refer to the onset of the intrinsic deflections in the respective curves. Standardization of the esophageal curves is illustrated in record *1*.

Conclusion: Left bundle-branch block.

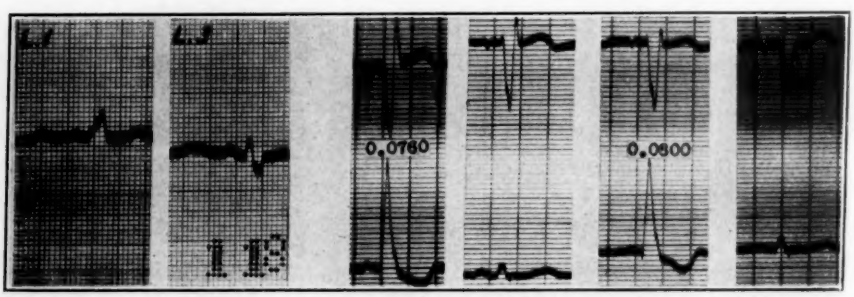

Fig. 18.—Patient E. W. Bundle-branch block of the common type though of low voltage. Single curves Leads I and III. In the double records the upper curves are from the esophageal electrode at 42, 40, 38.5, and 37 cm. depths, respectively, from left to right. Chest leads and Lead II are shown below. The numbers refer to times of onset of the intrinsic deflections in decimal fractions of a second in the esophageal curves.

Conclusion: Lag of the left ventricular base.

In the illustrations the times of onset of the chief upwardly directed deflections, signalling activation of the respectively adjacent muscle areas, have been indicated by decimal fractions of a second. These measurements have been placed below and near the beginning of the significant upward deflections in every instance. Figure 15 illustrates a typical result of applying the above procedure to a patient who showed no electrocardiographic sign of intraventricular block. The

accompanying Figs. 16 to 22, inclusive, demonstrate some of the results obtained by using this method in cases of intraventricular delay. Comments on detail are included in the legends to the illustrations.

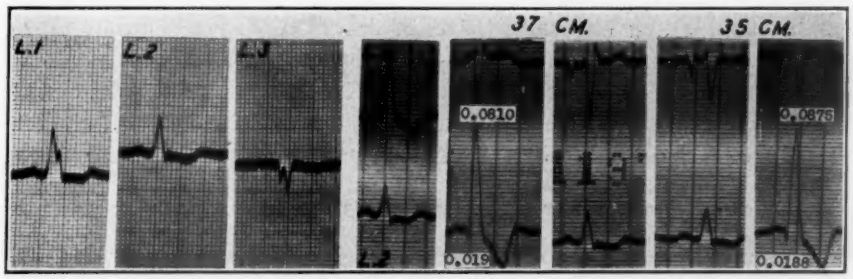

Fig. 19.—Patient M. G. Bundle-branch block of the common type. From left to right, single curves, Leads I, II, and III. From left to right, double curves, chest Lead V above and Lead II below. In the remaining curves the esophageal curves are the upper ones paired in turn with the chest lead, and Lead II at the depths of 37 and 35 cm. The numbers in fractions of a second indicate time of onset of the intrinsic deflections in the respective leads.
Conclusion: Left bundle-branch block.

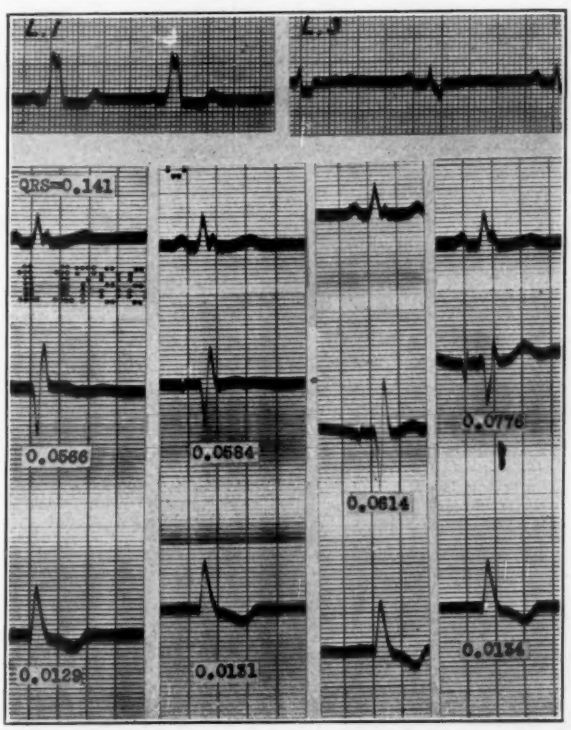

Fig. 20.—Patient H. I. Single records: Leads I and III. Triple records: Lead II above, esophageal curves in the middle, chest lead below. Numbers refer to onsets of the respective intrinsic deflections. The standardization of the exploring leads has been reduced to 1 mv. = 5 mm.
Conclusion: No lag of the left base. This is probably a bundle-branch block involving some part of the left ventricle other than the base.

The view is not entertained that the chief upward deflections in either the precordial or the esophageal tracings are exactly compar-

able in their time relations to the true intrinsic deflections as obtained by direct leads. The term "intrinsic deflection" is nevertheless used hereafter to describe the main upward strokes in semidirect curves since it has been proved by Wilson and his collaborators[68] and by experiments which have already been described (Fig. 14) that these indicate the approximate times of activation of the respectively explored areas. The esophageal lead is indeed only a modification of the approach of Wilson and his colleagues, but it is believed that the method offers a much more trustworthy guide to the intrinsic elec-

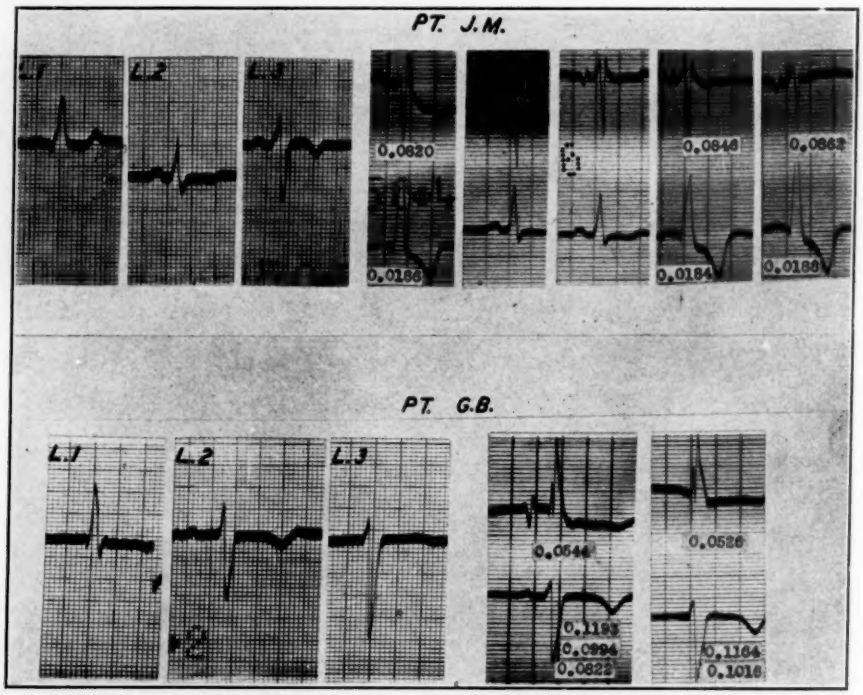

Fig. 21.—Patient J. M. From left to right single curves are Leads I, II, and III. Double curves, left to right: esophageal electrograms above at the depths 40, 40, 38, 38 and 36 cm., respectively, from the teeth, and below chest and conventional Lead II recorded simultaneously with the esophageal curves. The numbers denote the times of onset of the intrinsic deflections in esophageal and chest leads.

Conclusion: An example of left bundle-branch block.

Patient G. B. Left to right, single curves Leads I, II, and III and two examples of juxta-ventricular esophageal electrograms (above) recorded simultaneously with the precordial lead over the right ventricle. The numbers denote time of onset of intrinsic deflections in fractions of a second. Those pertaining to the right ventricle are placed opposite slurred components of the intrinsic deflection. The case is clearly one of right ventricular block. See text for discussion.

trical events in the basal portions of the left ventricle than can be obtained by chest leads. The view is held that the simultaneous use of both leads permits reliable conclusions to be drawn as to the order of activation of the ventricular areas underlying the electrodes.

In ten of the fourteen cases of bundle-branch block investigated by double semidirect leads unmistakable evidence was obtained of de-

layed activation of the left ventricle in the presence of early activation of the right. In two cases (see Fig. 20) there appeared to be no noteworthy lag in either of the explored areas although the QRS complexes as a whole were of abnormally long duration. The conclusion was reached that the interruption of conductivity in these cases must have affected some unexplored part of the ventricles, possibly in the anterior branches of the left bundle as emphasized by Mahaim.[41] Only one, rather atypical, example (Fig. 22) was found of the rare type (Wilson[68]) as judged by conventional Leads I and III (chief deflections in Lead I downward; in Lead III upward), and in this instance the semidirect leads indicated the presence of right bundle-branch block.

A very interesting result of the investigation is shown in Fig. 21 A and B. The conventional leads of these two patients show a general similarity, and yet the combined exploratory leads quite definitely show that in Fig. 21 A left ventricular block is present while in Fig. 21 B, there is delay in the activation of the right ventricle. The

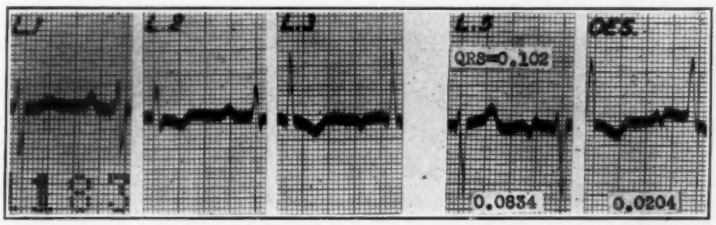

Fig. 22.—Patient R. M. An example of the rare type of bundle-branch block. From left to right, Leads I, II and III, chest Lead V, and juxta-ventricular esophageal lead. The chest lead shows obvious delay in the formation of the intrinsic deflection. The esophageal electrode in this case did not lie close to the left ventricular base, and the upstroke is therefore not a trustworthy indication of a true position of the intrinsic deflection. The conclusion is, however, warranted that this is a case of right ventricular block.

example also shows that bundle-branch block may occur without giving rise to the classical changes in the direction of the T-waves in standard Leads I and III.

Ventricular Extrasystoles.—Figure 23 is an example of the common type of bundle-branch block due to delayed activation of the left ventricle. One example of a ventricular extrasystole is marked by a cross in record 5. The time relationships of the onset of the intrinsic deflections in the extrasystolic electrograms are indicated on the record. It is evident that in this particular instance the base of the left ventricle was activated 0.0117 sec. in advance of the right ventricle in contradistinction to the sequence of events in the curve immediately preceding the extrasystole. Such a result leaves no room for doubt that the extrasystole must have arisen from a point in the left ventricle.

The procedure applied in Fig. 20 may be used as a useful method for locating the site of origin of ventricular extrasystoles. One ex-

ample of many studies pursued with this objective in view is illustrated in Fig. 24. The record exhibits curves of ventricular extrasystoles originating from three different foci. That in record 4 presumably arises in the septum, probably on the right side of the heart. It is, however, possible to argue that the triphasic precordial curve has been wrongly interpreted when the intrinsic deflection is assumed to occur at 0.029 sec. and that the true position of the intrinsic deflection in this instance arose nearer 0.086 sec. in the right ventricular area explored. This view is hardly tenable when the records 5 and

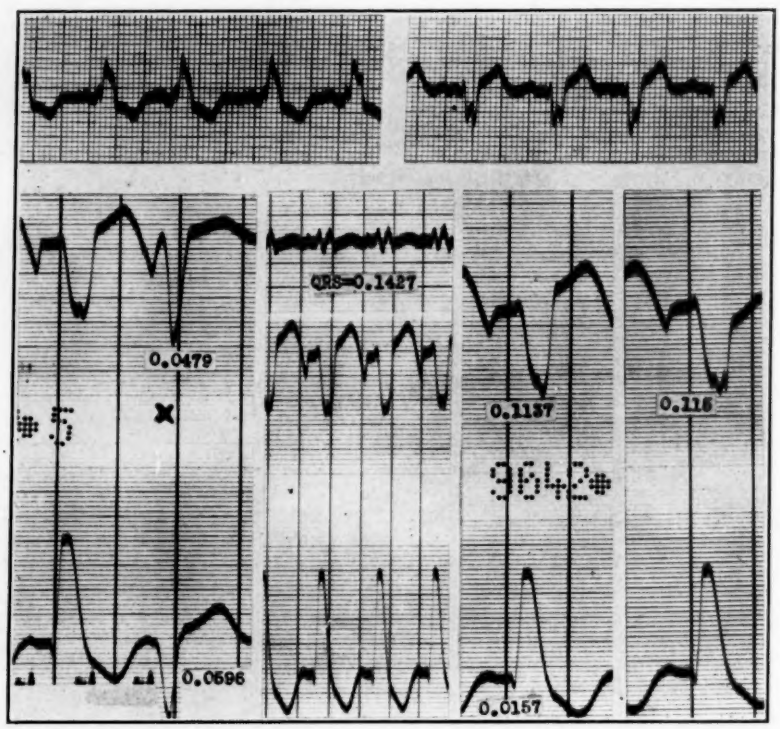

Fig. 23.—Patient B. J. Bundle-branch block of common type. Single string: Leads I and III. Double strings: esophageal curves above and chest curves below: camera at double speed. Triple strings: Lead II above, esophageal curve middle, and chest curve below; camera at usual speed. Numbers refer to onset of intrinsic deflections in decimal fractions of a second. An extrasystole is present in the first double record.

Conclusion: A clear example of left bundle-branch block with an occasional extrasystole, arising in the left ventricle.

7 are examined, for in these the extrasystoles arising from opposite sides of the heart yielded very characteristic changes in the appearance not only of the esophageal but also of the precordial curves. What is even more striking is that the conventional (Lead I) curves should be so similar in form in the presence of extrasystoles from opposite sides of the heart. The results of the adaptation of the esophageal lead to the study of ventricular extrasystoles suggest that

under the procedure described a more accurate conception of the meaning of conventional extrasystolic curves would be the reward of additional work in this field.

Conclusions on Bundle-Branch Block.—The employment simultaneously of two trustworthy exploring or semidirect leads to the two ventricles in fourteen cases of intraventricular block has thrown additional light upon the difficulties of accurate interpretation of standard electrocardiograms. The conventional leads of the majority of the cases (thirteen out of fourteen) were of the common type, and ten of these were shown to be associated with delay in activation of the base

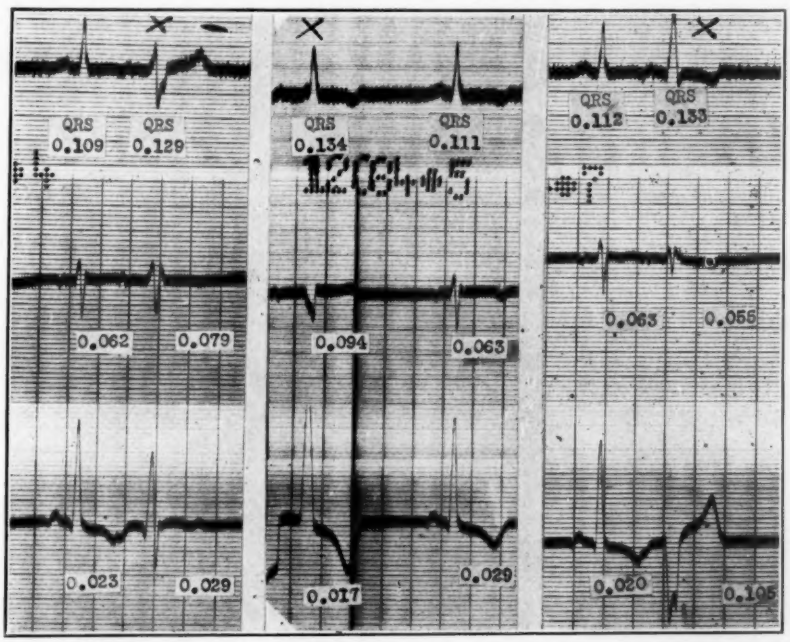

Fig. 24.—Patient M. McC. From a case exhibiting ventricular extrasystoles from three different foci. All three records were obtained with the esophageal electrode lying close to the base of the left ventricle. From above downward in each record are Lead I, an esophageal lead tapping the left ventricle, and a precordial lead over the right ventricle. The extrasystolic curves are indicated by crosses. The numbers in fractions of a second indicate the time of onset of intrinsic deflections. The ectopic beat in record 4, may have arisen from the right side of the septum. In record 5, the origin is clearly in the right ventricle and in record 7, in the left. The sensitivity of the string of the esophageal lead is reduced to one-third normal. In two of the records there is some distortion due to the tuning fork.

of the left ventricle. One fairly typical case of the rare type was due to right ventricular block. The occurrence of bundle-branch block does not necessarily give rise to "opposing T-waves." Right bundle-branch block may be present in cases showing conventional curves of the common type and therefore very likely occurs more often than is usually admitted under the new terminology. Two cases of the common type (as judged by the appearances of records of conventional Leads I and III) were probably of a "mixed" or "partial" variety.

Interpretations relying only on the basis of the directions of the main deflections in standard Leads I and III are not always reliable in indicating the site of the responsible lesion in bundle-branch block.

Summary of Section 5.—1. The reliability of the esophageal method when used as a semidirect or exploring lead to the left ventricle is discussed in the light of theoretical and experimental data.

2. The current interpretations of standard electrocardiographic leads in cases of bundle-branch block are set forth.

3. The results of employing simultaneous semidirect leads* with electrodes over the right and the left ventricles in bundle-branch block are illustrated and discussed.

4. Certain conclusions have been reached in view of the results obtained in a study of fourteen cases of intraventricular block.

5. The adaptation of simultaneous leads to the study of ventricular extrasystoles has yielded suggestive results.

GENERAL RECAPITULATION

The validity of using an electrode placed in the esophagus in clinical electrocardiography has been discussed at length in Section 1. On anatomical, theoretical, and experimental grounds the conclusion has been reached that, under the described procedure, the method may legitimately be applied to the human subject. In Sections 2 and 4 the findings in fifteen normal control subjects have provided the foundations upon which a detailed interpretation of the curves obtained by the esophageal lead have been based. As a result of experimental procedures on human and canine subjects, the conclusion has been reached that the esophageal lead is a trustworthy "exploring" or semidirect method. In this rôle it is subject to the general laws governing the employment of semidirect leads. The curves obtained by the method have been designated as "esophageal electrograms" since it has been shown that they have essentially the same characteristics as curves obtained by direct leads from the epicardial surface of the heart. The outstanding feature of esophageal electrograms is the demonstration of "intrinsic deflections" which signal the time of activation of the small areas of heart muscle lying immediately adjacent to the electrode.

The method has been applied to the study in 127 patients at the Johns Hopkins Hospital, exhibiting a wide range of cardiac disorders.

*The chest leads used in this study have without exception been derived with the right arm terminal on the precordium and the left leg terminal on the left leg. This arrangement ensures that electronegativity in the records obtained by the lead is indicated by an upward deflection. The use of the chest lead in an exploring rôle emphasizes the importance of maintaining this arrangement in spite of the recent agitation favoring a reversal of the electrodes in order to secure uniformity with the general appearance of the standard derivations. It is particularly desirable that the direction of the intrinsic deflections as obtained by all varieties of semidirect and direct leads employed in animal experimentation and clinical electrocardiography should conform to one rule.

The findings in 35 of these cases have been used in Sections 3 and 5 as a basis for discussion of the Ta-wave, ectopic auricular and ventricular extrasystoles, and bundle-branch block. The suggestion has been made that the esophageal lead may prove to be an aid to the location of the approximate site of origin of ectopic beats. Information of a precise character has been forthcoming with respect to the duration of the T-wave of the auricle in the human subject and its effect on conventional electrocardiograms. The findings in intraventricular delay largely support the new terminology although certain unexpected results and some examples of "mixed block" throw doubt upon the trustworthiness of the criteria which have generally been applied to the interpretation of bundle-branch block in man.

GENERAL SUMMARY OF PART I

I. From a theoretical and practical standpoint the validity of the use of the esophageal electrode as a type of semidirect lead in clinical electrocardiography has been established.

II. The results of employing the method in fifty human subjects have been recorded, analyzed and discussed.

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THROMBO-ANGIITIS OBLITERANS AND TOBACCO

The Influence of Sex, Race, and Skin Sensitivity to Tobacco on Cardiovascular Responses to Smoking*

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FROM clinical observations over a period of many years physicians have known that tobacco smoking was harmful to patients with thrombo-angiitis obliterans.[1, 2] A reason for the injurious effect was pointed out when, by means of skin temperature changes, we showed that tobacco smoking produced vasoconstriction of the vessels of the extremities[3, 4]; this process further decreasing the already impaired peripheral circulation of these individuals. This finding was corroborated and additional information was furnished by the work of Barker,[5] Wright and his associates,[6, 7, 8] and others.[9, 10]

Our investigation was continued to determine whether the observed cardiovascular effects of tobacco smoking had any peculiar features which might explain some of the unusual characteristics of thrombo-angiitis obliterans. Among the diseases in which tissues common to both sexes are involved, with the exception of hemophilia, no other condition shows the same almost entire predilection for males. Also, the frequence of the disease among individuals of the Jewish race is unusual. To throw some possible light on these oddities, the peripheral skin temperature, the pulse rate, and the blood pressure responses of male and female subjects and of Jewish and of gentile subjects to tobacco smoking were studied.

A second point of interest resulted from the excellent work on hypersensitivity to tobacco by Harkavy and his associates[11] and Sulzberger,[12] who showed that nearly 80 per cent of their group of patients with thrombo-angiitis obliterans gave an allergic skin reaction to tobacco; while less than half that number of responses was obtained among normal subjects. Sulzberger considers the evidence to be highly suggestive that thrombo-angiitis obliterans is connected in some way with a hypersensitivity to tobacco, since in agreement with his experimental data he finds many clinical features of thrombo-angiitis obliterans which are common to other allergies. It is known, for example, that certain allergens involve certain tissues and even that tissue in certain definite areas only. Thus tobacco may affect the vascular apparatus, especially in the extremities, and produce changes in the blood vessels themselves and the tissues supplied by them. We were interested in knowing whether individuals who showed a skin sensitivity to tobacco extract

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had a greater peripheral vasoconstrictor effect from tobacco smoking than individuals who were not skin sensitive.

PROCEDURE

All of the healthy young adult subjects were studied under the same conditions. The males were medical students who smoked from fifteen to twenty cigarets a day. The use of cigarets by the females was not so uniform. No smoking was permitted for a period of three hours before the test. To keep normal peripheral vasoconstriction at a minimum,[4] the room in which the study was carried out was kept at a temperature of 85° F. ± 3°. In order that the skin temperatures of the subjects, who were studied lying on a comfortable bed, could rapidly reach an adjustment to the environmental conditions, their arms and legs were bared while their trunks were covered with only single sheets. The smoking period for two cigarets of the standard brand used throughout the test was twenty minutes. Usually two-thirds of one cigaret was consumed in from seven to nine minutes, then there was a pause for two or three minutes, then a second cigaret was smoked in the same time as the first one. Skin sensitivity to tobacco was determined by the intradermal technic. The tobacco solution was a composite one combining several different brands of tobacco. Coca's control solution was used on the opposite forearm. The reaction was considered to be one-plus when the original wheal enlarged to from 8 to 11 mm. in diameter, two-plus from 12 to 14 mm., three-plus from 14 to 17 mm., four-plus from 17 mm., or any size above, or the development of pseudopods. At five-minute intervals the skin temperatures of the tips of the left fingers and toes were recorded with a Tycos dermatherm, the blood pressure in the right arm was taken with a standard sphygmomanometer, and the pulse rate was counted for one-half minute.

DATA AND COMMENT

A typical example of the decrease in the peripheral skin temperature and increase in blood pressure and pulse rate on smoking is shown in Fig. 1. The data from a study of twenty-nine subjects are given in Table I.

Influence of Sex.—Cigaret smoking produced a decrease in the skin temperatures of the fingers and toes and an increase in the pulse rates and blood pressures in women to the same degree that it did in men.

In the light of the relation of tobacco smoking to thrombo-angiitis obliterans this fact offered no explanation as to why the disease shows the marked predilection for males. If smoking is the cause of thrombo-angiitis obliterans, one would expect to see this disease appear more frequently in women in the future because there is no doubt but that they are smoking more than did past generations of their sex. On the other hand, the possibility of a sex hormone in some way protecting the

TABLE I

SUMMARY OF CARDIOVASCULAR EFFECTS OF SMOKING TWO CIGARETS

SUBJECT NUMBER	AGE	DAILY USE OF CIGARETS	INHALES	SKIN SENSITIVITY TO TOBACCO	DECREASE IN AVERAGE SKIN TEMP. OF FINGERS	DECREASE IN AVERAGE SKIN TEMP. OF TOES	INCREASE IN PULSE RATE PER MIN.	INCREASE IN BLOOD PRESSURE (MM. HG.) SYSTOLIC	DIASTOLIC
				Males—Gentiles					
1	25	15	D*	Neg.	0.4° C.	1.2° C.	22	6	8
2	26	20	D	Neg.	1.1	3.4	16	8	6
3	23	20	D	Neg.	1.2	0.9	18	12	6
4	23	15-20	M	Neg.	1.2	1.1	22	24	16
5	24	15	M	Neg.	0.3	1.2	18	14	20
6	22	15-20	M	Neg.	0.8	1.0	16	16	14
				Average	0.8	1.5	19	13	12
7	23	20	D	++++	0.5	2.5	10	12	10
8	21	15	D	++++	0.5	1.4	12	6	6
9	33	20	M	+	2.1	2.5	14	16	12
10	23	15	M	++++	1.1	1.7	16	14	16
11	26	24	M	++	0.8	1.9	14	16	6
12	23	15-20	M	++++	6.3	1.8	14	10	8
				Average	0.9	2.0	13	12	10
				Males—Jewish					
13	25	25-30	D	Neg.	0.9	2.3	24	14	6
14	26	30	D	Neg.	2.4	2.9	12	12	8
15	24	35-40	D	Neg.	4.6	4.0	24	18	10
16	23	15	M	Neg.	1.5	2.3	24	10	14
17	23	15	M	Neg.	2.8	3.7	28	8	12
18	23	15-20	M	Neg.	0.6	0.9	16	18	14
19	25	10-12	S	Neg.	1.4	4.8	14	10	12
				Average	2.0	3.0	20	13	11

*D = Deeply
M = Moderately
S = Slightly

TABLE I—CONT'D

SUBJECT NUMBER	AGE	DAILY USE OF CIGARETS	INHALES	SKIN SENSITIVITY TO TOBACCO	DECREASE IN AVERAGE SKIN TEMP. OF FINGERS	DECREASE IN AVERAGE SKIN TEMP. OF TOES	INCREASE IN PULSE RATE PER MIN.	INCREASE IN BLOOD PRESSURE (MM. HG.) SYSTOLIC	DIASTOLIC
20	25	15	M	+++	1.9	4.3	12	10	10
21	25	20	M	++++	1.2	1.6	20	20	8
22	22	20	D	++	5.4	3.2	18	16	20
				Average	2.8	3.0	17	15	13
				Females—Gentile					
23	27	2-3	S	Neg.	1.5	2.3	16	10	14
24	35	2-3	S	Neg.	0.8	0.8	14	8	12
25	22	10-12	M	Neg.	2.2	2.8	20	10	8
26	22	10	M	Neg.	2.4	3.1	30	14	16
27	16	8-10	M	Neg.	1.6	2.0	12	22	12
28	18	10-15	M	Neg.	0.6	1.6	24	12	16
29	20	10-15	M	+	1.6	3.6	14	16	18
				Average	1.5	2.3	19	13	14

females must be kept in mind, since McGrath[13] has shown that large doses of theelin kept female rats from developing gangrene of the tail when toxic quantities of ergotamine tartrate, a vasoconstrictor substance, were given.

Influence of Race.—The average decrease in the skin temperatures of the fingers and toes and the average increase in blood pressures and pulse rates were greater for the Jewish males than for the gentile males. The difference was particularly more marked in the skin temperature changes.

The reason for this difference between the two groups is not entirely apparent. It would be easy to assert that this fact is responsible for

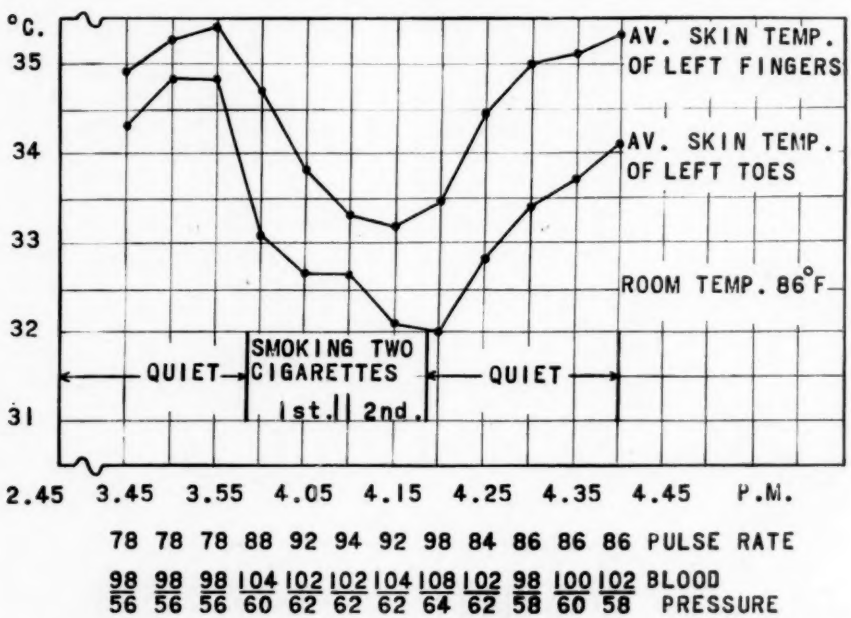

Fig. 1.—Decrease in the skin temperature of the fingers and toes and increase in pulse rate and blood pressure of Subject 25, female, on the smoking of two cigarets.

the greater incidence of thrombo-angiitis obliterans in Jews than in other elements of the population; but tobacco smoking has not been definitely established as the cause of that disease. It is possible that a simpler reason is the true one. We were impressed by the fact that the smoking of the Jewish subjects was more intensive, was quicker, and with deeper inhalations than that of the gentile subjects. This temperamental difference may be the factor accounting for the greater cardiovascular response among Jews, since slow smoking and simple puffing rather than inhaling is known to produce a lesser effect.[4] Hypersensitivity to tobacco could not have been the cause of the race difference, as skin reactions to tobacco were twice as frequent among the gentiles as among the Jews.

Influence of Hypersensitivity to Tobacco.—There was no consistent difference in the skin temperatures, the blood pressure, and pulse rate response to smoking between individuals who showed skin sensitivity to tobacco and those who did not. In accord with this, among the sensitive individuals there was no correlation between the degree of the skin reaction and the cardiovascular response. This finding is a corroboration of a preliminary report on the same question by Wright and Moffat.[8]

We consider the lack of relationship between skin sensitivity to tobacco and the cardiovascular response to smoking to be due to the fact that the two effects are the result of different components. Sulzberger[12] has emphasized that the reaction of hypersensitivity is produced by a constituent or constituents of tobacco other than nicotine. In contrast to this, we found[4] that nicotine administered intravenously in amounts theoretically absorbed in the smoking of one or two cigarets produced approximately the same decrease in the skin temperature of the fingers and toes and the same increase in blood pressure and pulse rate as was obtained on the smoking of one or two cigarets. In further support of the theory that the nicotine component is responsible for the peripheral vasoconstriction, the mechanism by which tobacco smoking causes a drop in the skin temperature of the extremities is of interest. It is claimed[14, 15] that the effect of nicotine is largely brought about through the sympathetic nervous system. That the peripheral vasoconstrictor effect of tobacco observed by us was carried out through the nerve supply to the part was demonstrated by anesthetizing the test area, the toes, on one foot by a posterior tibial nerve block and obtaining no decrease in their skin temperature on smoking, while the usual decrease occurred in the unanesthetized toes of the other foot. That the sympathetic fibers were the pathways involved was shown by obtaining, on smoking, no decrease in the skin temperature in the toes of a subject who had had a bilateral lumbar sympathetic ganglionectomy, while the usual response occurred in the unaffected fingers. Thus the peripheral vasoconstrictor effect of tobacco smoking is carried out through the same mechanism by which nicotine acts.

It is not necessary to consider the allergic possibilities of tobacco to understand its aggravating action in thrombo-angiitis obliterans. In a disease which is characterized by a deficiency in circulation due to thromboses and in which a substance is known clinically to be detrimental, the production of vasospasm by that substance would seem to be a significant effect and much more direct than an allergic effect. The vasoconstrictor effect is so pertinent to this occlusive arterial disease that one cannot say definitely that tobacco is not the exciting cause of thrombo-angiitis obliterans, as it is claimed to be by Silbert.[2] Other vasoconstricting substances, pituitrin,[16] and particularly ergot[17] have

been responsible for peripheral gangrene. There is thus considerable evidence that prolonged or marked vasoconstriction may initiate organic vascular occlusions.

Gaps still exist in the knowledge of thrombo-angiitis obliterans, but the fact has been established that cigaret smoking reduces the blood supply to the extremities; and one should not hesitate to present the reasons for the avoidance of tobacco and to order "no smoking" by patients with that disease.

SUMMARY

1. The smoking of two cigarets by women resulted in a drop in the skin temperatures of their fingers and toes, and in an increase in their blood pressures and pulse rates similar to those observed in men.

2. Such cigaret smoking by Jewish males caused a greater drop in the skin temperatures of their fingers and toes than occurred in gentile males. This fact may be of significance in accounting for the greater incidence of thrombo-angiitis obliterans among Jews than among other elements of the population.

3. No relationship was found between skin sensitivity to tobacco and its cardiovascular effect on smoking.

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THE RELATION OF THE SYSTOLIC BLOOD PRESSURE AND HEART RATE TO ATTACKS OF ANGINA PECTORIS PRECIPITATED BY EFFORT* †

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ALTHOUGH angina pectoris is a disorder of the cardiovascular system, our knowledge of the changes in the circulation accompanying attacks is very meager. The standardized exercise tolerance test recently described[27] affords a means of inducing typical paroxysms of angina and makes possible accurate measurement of the heart rate and blood pressure during various phases of the paroxysms.

Measurements of the heart rate and systolic blood pressure were made in thirty-five patients before and during induced attacks of angina, in order to learn whether the changes which occurred were of any diagnostic or etiological importance and to learn whether the disappearance of angina pectoris following total thyroidectomy was dependent on a diminished internal secretion of adrenalin.

METHODS

Attacks of angina pectoris were induced by exercise under standard conditions according to the method previously described.[27] The test was performed in a room maintained at a temperature between 45 and 55° F. The exercise consisted of repeatedly mounting and descending a staircase made up of two steps, each nine inches high; the duration of exercise being limited in each patient by the development of anginal pain. The patients were allowed to work at a rate which was natural and comfortable for them.

All patients were accustomed to the test and the apparatus before the measurements were made. The number of trips and the duration of exercise which induced angina in these tests did not differ appreciably from that required when determining the exercise tolerance of the same patients without the apparatus for determining blood pressure and heart rate.

The resting heart rate and systolic blood pressure were measured at one-minute intervals with the patient standing at ease; thereafter measurements were made at one-half-minute intervals throughout the exercise, during the induced attack of angina, and during the period of recovery. The systolic blood pressure was determined by palpation, using a standard cuff attached to the right arm and connected by rubber

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tubing to a mercury manometer on a nearby table. The results obtained by this method were found to agree satisfactorily with measurements of the blood pressure obtained by the auscultatory method during exercise on the staircase or on the bicycle ergometer. The heart rate was obtained by the use of a stethoscope strapped to the precordium, the number of beats in fifteen seconds being counted. The results obtained by this method were found to agree satisfactorily with simultaneous heart rate measurements obtained from electrocardiographic tracings obtained during exercise. Duplicate determinations on different days revealed only minor variations in the heart rate and blood pressure curves.

Measurements made using the bicycle ergometer showed the same types of changes in heart rate and systolic blood pressure as were observed when angina was induced by exercise on the two-step staircase. Because of the difference in the two types of work, however, there are differences in the actual heart rate and blood pressure readings obtained by these two methods.

RESULTS

Thirty-five patients who developed angina pectoris on exertion and fifteen individuals of similar age (forty-five to sixty-five years), but with no evidence of heart disease, were studied. Measurements made before and after entering the cold room showed that the temperature had no appreciable effect on either the heart rate or the blood pressure.

The number of trips necessary to induce angina in the different patients ranged from nine to sixty-four. Ten of the thirty-five patients with angina developed a typical attack after less than two minutes of exercise; fourteen exercised from two to three minutes before pain forced them to stop; and the remaining eleven were able to exercise for three and one-third to four and one-half minutes. The rate of exercise was twelve to eighteen trips per minute in twenty-one patients, nine to eleven trips per minute in twelve patients, and twenty to twenty-two trips per minute in two patients.

TABLE I

THE INCREASE IN HEART RATE WITH ATTACKS OF ANGINA PECTORIS

INCREASE IN HEART RATE (BEATS PER MIN.)	AT ONSET OF ANGINAL ATTACK (NUMBER OF CASES)	DURING ATTACKS* (NUMBER OF CASES)
-10 to + 9	0	3
+10 to +19	0	5
+20 to +29	2	6
+30 to +39	5	8
+40 to +49	9	2
+50 to +59	5	4
+60 to +69	3	2
+70 to +79	4	0
+80 to +89	3	0
Total	31	30

*One minute after cessation of exercise.

There was no appreciable difference between the curves of heart rate and systolic blood pressure during and after exercise of those patients who developed angina on exertion and those normal persons who undertook the same exertion but who did not develop heart pain.

The heart rate during exercise was studied in thirty-one of the patients with angina pectoris and in thirteen of the persons with no heart disease. In general the heart rate increased steadily during exertion, reached a maximum after approximately two or three minutes of exercise, and decreased rapidly during recovery (Table I). The curves showing the average increase in rate for each half minute of exercise and recovery in thirty-one patients with angina pectoris and ten patients with no heart disease appear in Fig. 1. The rate at which the heart rate increased during exertion varied somewhat in the different patients.

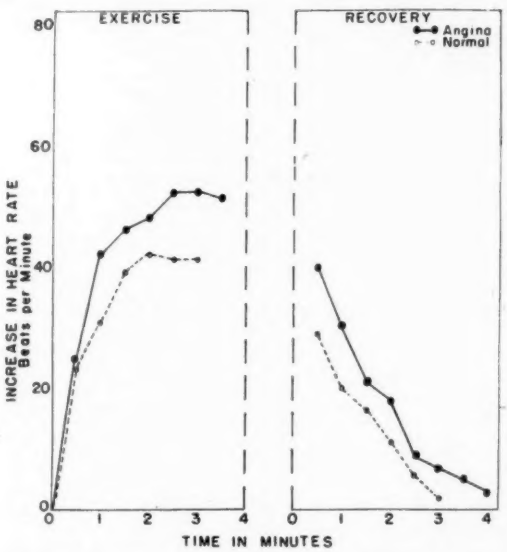

Fig. 1.—The average increase in hear rate during exercise and recovery of thirty-one patients who developed angina pectoris on exertion and in thirteen persons with no evidence of heart disease. The duration of time between the last measurement made during exercise and the first measurement during recovery was 30 seconds.

This variation was apparently unrelated to the variation in the heart rate at rest, the development of angina pectoris, or the speed of exercise in these tests. Although the average increase in heart rate for patients with no evidence of heart disease was slightly less than the average for patients with angina pectoris, individual patients in both groups showed curves which were very similar.

In seventeen of the thirty-one patients with angina pectoris the increase in heart rate for each half minute of exercise was within twelve beats per minute of the average increase for all patients with angina. In these individuals the heart rate, at the time pain developed, was forty to sixty-eight beats per minute greater than the rate at rest. Pa-

tient 29 (Fig. 2) is typical of this group, while D. O., of the normal group, showed a similar response. In six other patients with angina the increments were definitely less than average, so that at the time pain developed the heart rate had increased only 28 to 36 beats per minute. Patient 27 (Fig. 2) of the angina group and J. R., of the normal group, are representative of this type of response. In the remaining eight patients with angina pectoris the heart rate showed a response that was strikingly greater than average. At the time that angina developed the heart rate was 74 to 80 beats per minute higher than the resting level (Patient 23, angina, and E. W., normal, Fig. 2).

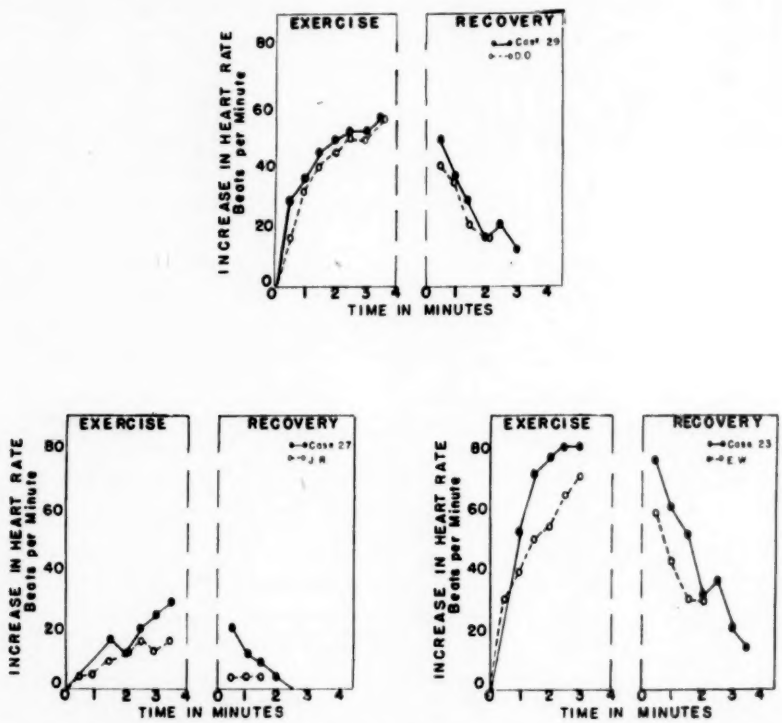

Fig. 2.—Characteristic changes in heart rate during and after exercise in patients who developed angina pectoris on exertion and in persons with no evidence of heart disease. The duration of time between the last measurement made during exercise and the first measurement during recovery was 30 seconds.

The shape of the curve was not altered by the onset of anginal pain. Two patients who developed heart pain and one person with no heart disease showed premature beats during the exercise and for a short time following exertion.

With the cessation of exercise the heart rate decreased rapidly. During the first minute of recovery the average decrease in heart rate was 23 beats per minute. The length of time necessary for the heart to return to the resting rate varied considerably, and, although not determined in all instances, two minutes were required in about one-half the

cases, while in a few instances as long as four and one-half minutes were necessary (Table I). The continuation or rapid disappearance of anginal pain was apparently unrelated to the rate of slowing of the heart.

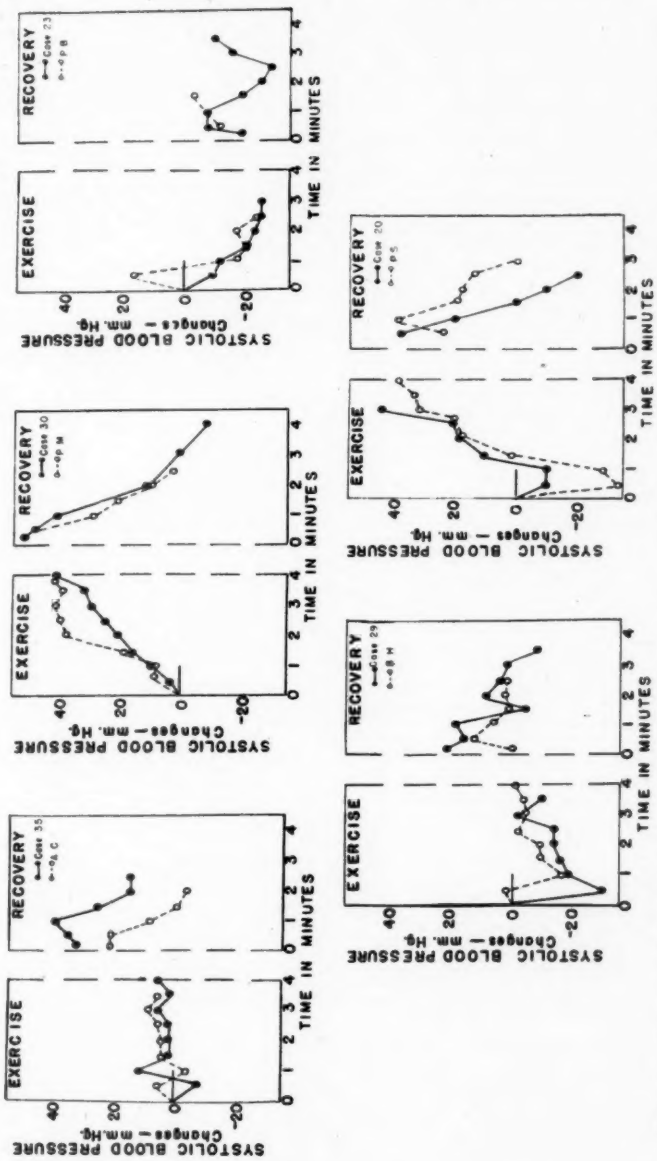

Fig. 3.—Characteristic changes in blood pressure during and after exercise in patients who developed angina pectoris on exertion and in persons with no evidence of heart disease. The duration of time between the last measurement made during exercise and the first measurement during recovery was 30 seconds.

The systolic blood pressure showed five types of response during exercise. The type of response for a given individual was quite constant and was not influenced by the blood pressure during rest nor the rate of exercise. Similar types of response were observed in both the patients

with angina pectoris and those without heart disease. The shape of the curve was not altered by the onset or presence of heart pain.

Group 1. In seven patients with angina pectoris there was little or no change during exercise, the blood pressure remaining within 10 mm. Hg of the resting level, e.g., Patient 35, angina pectoris (Fig. 3) and A. C., normal (Fig. 3). *Group 2.* In seven instances the blood pressure gradually increased 16 to 44 mm. Hg above the resting level, e.g., Patient 30, angina pectoris (Fig. 3) and P. M., normal (Fig. 3). *Group 3.* In six patients with angina the blood pressure dropped steadily during exercise, reaching its lowest level (20 to 38 mm. Hg lower than the resting level) when angina developed, e.g., Patient 23 (Fig. 3). Four of these patients developed angina after less than two minutes of exercise; P. B., with no heart disease, showed a similar blood pressure curve (Fig. 3). *Group 4.* Seven patients with angina showed a drop of 10 to 24 mm. Hg during the first minute of exercise, similar to what occurred in Group 3. The pressure then increased, approached, and later exceeded the resting level so that at the time of development of heart pain the pressure was 10 to 44 mm. Hg higher than the level during rest, e.g., Patient 20 (Fig. 3) and P. S. (Fig. 3). *Group 5.* In eight of the thirty-five patients with angina there was an initial drop in pressure during the first minute varying between 16 and 60 mm. Hg similar to Groups 3 and 4. This was followed by a slow and gradual rise which approached, but did not exceed, the resting level despite exercise which continued for as long as four minutes, e.g., Patient 29 (Fig. 3) and B. H. (Fig. 3).

The systolic blood pressure at the onset of the attack was in some cases higher, in others lower, and in many instances essentially the same as the blood pressure during rest (Table II). This variation was brought about by two factors: (1) the changes in blood pressure caused by exercise and (2) the duration of the exercise before being terminated by the onset of pain.

After the cessation of exertion there was usually a sharp rise in the systolic blood pressure, reaching a maximum within the first one and one-half minutes of recovery. This maximum was usually, but not always, higher than the level observed at any time during exercise or during rest (Table II). The blood pressure then gradually fell and returned to the resting level in about one and one-half to four minutes

TABLE II

THE CHANGE IN SYSTOLIC BLOOD PRESSURE WITH ATTACKS OF ANGINA PECTORIS

CHANGE IN SYSTOLIC BLOOD PRESSURE (MM. HG)	AT ONSET OF ANGINAL ATTACK (NUMBER OF CASES)	DURING ATTACK* (NUMBER OF CASES)
+11 to +68	13	26
±10	14	7
−12 to −38	8	1
Total	35	34

*From 30 to 90 seconds after cessation of exercise.

(Fig. 3). This elevation in systolic blood pressure following exercise was independent of the continuation or disappearance of anginal pain and occurred in patients who did not develop angina on similar exertion.

Effect of Total Thyroidectomy

Changes in systolic blood pressure and heart rate during exercise were studied in eleven patients with angina pectoris before and after total ablation of the thyroid (Table III). In seven of the eleven cases the lowering of the metabolism induced by this procedure was accompanied by relief from symptoms as evidenced by the clinical history and an increase in exercise tolerance. Three of these seven patients (Cases 17, 30, 33) were able to exercise indefinitely without experiencing angina, the test being discontinued usually after ten to twenty minutes of work. The remaining four patients (Cases 32, 27, 12, 3) developed no angina but were forced to stop because of fatigue after performing more than twice as much exercise as was possible before operation. In four patients (Cases 5, 10, 24, 25) there was little or no improvement as judged by the clinical history and the exercise tolerance test. These individuals had low basal metabolic rates or other signs of low metabolism before operation. Experience has shown that such patients are not helped by thyroidectomy, for further lowering of the metabolism is not compatible with comfort.

The heart rate was studied in nine patients, four of whom showed little or no improvement following the operation, and five of whom showed varying degrees of benefit (Table III). During the prolonged exertion that was made possible in the latter five patients the heart rate increased as much as, or more than, it did before operation (Fig. 4). With this increased exertion the total number of beats per minute during exercise was greater than before operation in three individuals, and smaller in two. In both of the latter cases the heart rate at rest was lower after operation than preoperatively.

The amount of exercise which induced angina preoperatively caused the same increase in heart rate both before and after operation in five patients, three of whom were improved by the operation and two of whom showed no improvement. In two patients, one of whom showed clinical improvement, this amount of work caused a greater increase after operation, and in two patients, one of whom was improved (Fig. 4), the increase in heart rate was less postoperatively. The degree of clinical improvement, therefore, was unrelated to the response of the heart rate during exertion.

The systolic blood pressure after total thyroidectomy was studied in all eleven patients (Table III). Comparable amounts of exercise did not cause as great a rise in blood pressure after operation as preoperatively (Table III, Fig. 4). Prolonged exertion in the seven patients who showed clinical improvement was accompanied by the same or a

TABLE III

CASE NO.	TIME OF TEST	BASAL METABOLIC RATE (%)	DURING REST HEART RATE (BEATS PER MIN.)	DURING REST SYSTOLIC BLOOD PRESSURE (MM. HG)	DURING EXERCISE HEART RATE (BEATS PER MIN.)	DURING EXERCISE SYSTOLIC BLOOD PRESSURE (MM. HG)	DURATION OF EXERCISE (MINUTES)	HEART RATE (BEATS PER MIN.)	SYSTOLIC BLOOD PRESSURE (MM. HG)	EXERCISE TOLERANCE (MIN.)	REMARKS
5	Before operation	−14	86	150	142	146	1.4				Anginal attack
	After operation	−36	76	202	132	180	2.5				Anginal attack
10	Before operation	−24	84	142	160	160	1.8				Anginal attack
	After operation	−30	112	124	152	120	3.2				Anginal attack
24	Before operation	−17	104	128	144	146	3.0				Anginal attack
	After operation	−37	80	152	144	158	4.0				Anginal attack
25	Before operation	?*	80	126	132	108	3.3				Anginal attack
	After operation	−46	68	126	116	116	3.5				Anginal attack
32	Before operation	+ 5	92	132	152	170	4.0				Anginal attack
	After operation	− 5*	80	168	144	168	5.5				No angina
27	Before operation	−19	64	136	92	174	3.5				Anginal attack
	After operation	−33	60	220	120	200	3.5	124	212	6.7	No angina
12	Before operation	+ 3	124	158	168	180	2.3				Anginal attack
	After operation	− 3*	112	172	144	174	2.5	160	190	7.8	No angina
3	Before operation	− 7		112		80	1.3				Anginal attack
	After operation	−34		172		144	1.5		172	3.9	No angina
17	Before operation	−15	64	164	112	160	2.5				Anginal attack
	After operation	−29	56	146	104	140	2.5	128	162	19.5	No angina
30	Before operation	− 4	104	148		190	3.8				Anginal attack
	After operation	−18	86	148		216	4.0		220	10.0	No angina
33	Before operation	− 7	92	214	148	222	4.0				Anginal attack
	After operation	−29	100	210	156	206	4.0	160	220	20.0	No angina

*These patients had blood serum cholesterol of 300 mg. or more or other evidences of clinical myxedema.

greater increase in blood pressure and the same or a definitely higher level of systolic blood pressure, but no precordial discomfort. With the cessation of exercise several patients showed a further increase in systolic pressure similar to that which they showed before operation and similar to that which occurred in patients with no heart disease.

Adrenalin, like exercise, causes an increase in blood pressure and heart rate. The response to intravenous injection of adrenalin before and after total thyroidectomy has been the subject of a previous communication.[28] In four patients of the present series both the response to adrenalin and the response to exercise were studied.

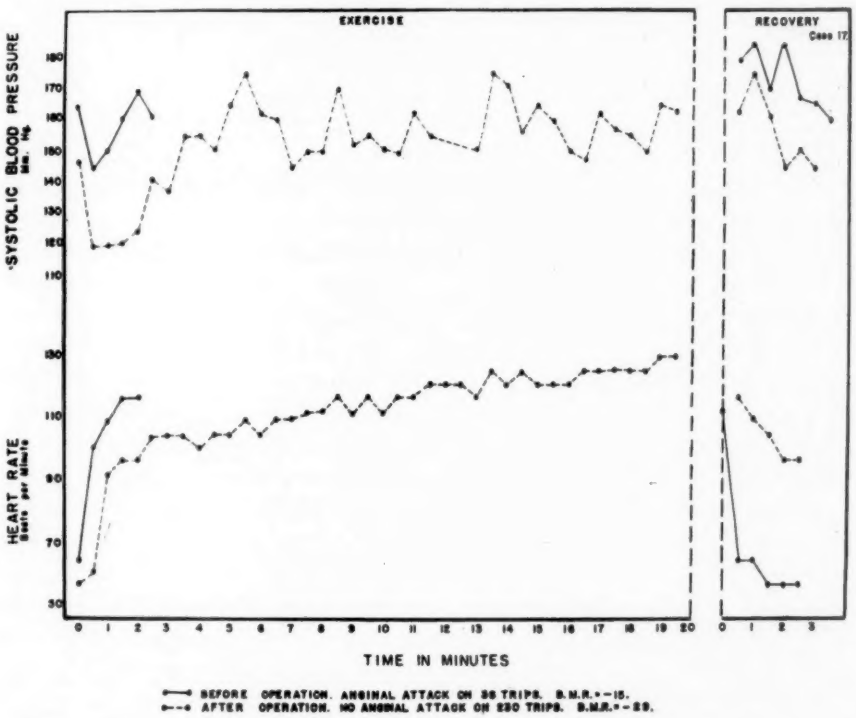

Fig. 4.—Changes in heart rate and blood pressure during exercise before and after total thyroidectomy. The duration of time between the last measurement made during exercise and the first measurement during recovery was 30 seconds or less.

The preoperative basal metabolic rate in Case 17 was –15 per cent and thirty-six trips over the staircase induced angina (Fig. 5). One week following operation, before the basal metabolism was lowered, forty-two trips failed to induce cardiac pain. This early relief of pain is due to interruption of afferent nerve pathways at the time of operation and is a temporary phenomenon.[33] In this patient the basal metabolic rate was maintained at the preoperative level by the administration of thyroid extract for three weeks, at which time thirty-six trips again induced angina. Thyroid extract was then omitted. Eight weeks after opera-

tion the basal metabolism was –29 per cent, and the patient had improved so that he was free of pain even after two hundred trips. The response of the blood pressure and heart rate to adrenalin and to thirty-six trips of exercise was essentially the same as before operation. Continuation of the exercise, however (two hundred trips), caused a sharp rise in blood pressure and a further increase in heart rate. At a later date (twelve weeks after operation) severe myxedema developed. At this time there was a marked decrease in the sensitivity to adrenalin, for relatively large doses (3.5 c.c. per minute of 1:100,000 solution) were required to induce the same change in blood pressure and heart rate as had previously been produced by much smaller doses (1.0 c.c. to 1.4 c.c. per minute of a 1:100,000 solution). The response of the heart rate and blood pressure, however, was essentially unchanged. Similar results were observed in the other three patients.

COMMENT

The lack of knowledge regarding circulatory changes associated with attacks of angina pectoris is largely due to the fact that the attacks are brief, and supervene without giving sufficient warning to allow preparation for careful, adequate study. Although several investigators have had the opportunity to measure the heart rate or blood pressure while the pain still persisted, such opportunities are rare and are largely beyond control. The lapse of time from the onset of the attack to the time when measurements can be made necessarily varies in different instances, and the normal heart rate and blood pressure for comparison must necessarily be determined at a subsequent time or from records of previous examinations. Such measurements give little information as to the behavior of the circulation at the very onset or immediately preceding the attacks when changes in the circulation might possibly be of importance in inducing the paroxysm. The rapid development, relatively short duration, and rapid disappearance of the paroxysms of pain suggest that there may be an equally rapid progression of changes in the circulation, and a single determination of the heart rate or blood pressure, therefore, fails to give an adequate picture of the circulatory changes accompanying the various phases of the attack.

Attacks of angina pectoris have been induced experimentally by adrenalin,[16, 18] anoxemia,[17, 29] and exercise.[3, 25, 26, 27, 31, 32, 36] The ability to induce attacks of angina at will enables one to prepare for careful observation and to observe the entire chain of events during the development, duration, and disappearance of the pain. The significance of such measurements in relation to attacks of angina pectoris as they occur clinically depends largely on how closely the induced attacks correspond to spontaneous attacks, both in clinical characteristics and in etiology. While the precipitation of attacks of angina pectoris by adrenalin or anoxemia has no close clinical counterpart, the induction of attacks by

exertion is natural and in fact is one of the characteristic clinical features. The standardized exercise tolerance test previously described[27] duplicates faithfully the conditions under which many attacks are precipitated in normal life. By means of this test it is possible to induce paroxysms of angina in the vast majority of patients suffering from this condition, and the clinical characteristics of the attacks so induced are identical with those usually experienced by the patient in daily life. The ability to induce typical attacks of angina under these controlled conditions makes it possible to measure accurately the heart rate and blood pressure before the attack, during the development and onset of the paroxysm, during the height of the pain, and during the recovery from the attack. The necessity for rapidly repeated measurements is clear when one observes the swift succession of changes in the circulation which take place during the precipitation and recovery from attacks of angina. Striking changes in heart rate and blood pressure are evident within a few seconds after the cessation of exercise; observations made "during the attack," therefore, give little insight into the situation at the onset or immediately preceding the paroxysm.

Observations of the systolic blood pressure and heart rate before, during, and after paroxysms of angina pectoris, induced by exercise, reveal no characteristic changes which might aid in establishing the diagnosis. Bischoff,[3] Wasserman,[31] Portocalis and Flora,[25] Wood and Wolferth,[36] and Wayne and Laplace[32] have induced attacks of angina by means of effort and measured the heart rate and blood pressure "during the attack" within a few moments after cessation of the exertion. Under such conditions the heart rate and the blood pressure were elevated in most, although not in all, patients.[36]

The elevation of blood pressure under such conditions is a normal reaction which takes place during the first few minutes of recovery from exercise and is a result of the exercise, not of the angina. A similar rise in blood pressure following exercise has been observed in a group of normal patients studied by Cotton, Rapport, and Lewis[9]; our control group, with no evidence of heart disease, showed this same reaction; a similar response was observed in the group treated by thyroidectomy who no longer developed pain on exertion; and a similar reaction was seen in patients with angina pectoris who stopped exercise before the attack was precipitated.

An entirely different picture is seen if the measurements are made at the time of onset of the anginal attack or immediately before the onset of pain; the systolic blood pressure at this time is higher in some patients, lower in others, while in still others the blood pressure is essentially the same as it was during rest (Table II).

The heart rate at the onset of attacks of angina induced by exertion is elevated, as might be expected from the nature of the stimulus employed in inducing the pain. The degree of elevation is of no aid in

establishing the diagnosis, for it varies in different patients regardless of the presence or absence of angina pectoris.

The attacks of angina pectoris are not induced by any characteristic changes in systolic blood pressure or heart rate. Observations of the blood pressure during paroxysms which develop spontaneously with the patient at rest reveal little agreement as to the changes in blood pressure under such conditions. Hunter,[15] Burgess,[8] and Levine and Ernstene[19] have found the blood pressure higher during attacks of angina than at other times. Levine and Ernstene suggest "that a temporary elevation in blood pressure is an important factor in the production of anginal attacks and may even be a necessary immediate cause of the attack."[19] Allbutt[1] cites two cases with elevated blood pressure and one with depressed blood pressure during attacks. Mackenzie[22] and Lewis[21] have presented an unusual group of cases with aortic regurgitation in which attacks of angina were ushered in by a rise in systolic blood pressure. Regarding such cases, Mackenzie states, "Although I have taken blood pressure observations in cases of angina pectoris during the attack, no others have been found which show . . . the rise in pressure consistently associated with recurrence of pain."[23]

The observations made in the present study show that the systolic blood pressure at the onset of attacks of angina is not always elevated but may be lower or essentially the same as the blood pressure during rest. These measurements were made during attacks induced by conditions which precipitate a large proportion, if not the great majority, of attacks which occur clinically. The observations recorded, therefore, show that such paroxysms of angina are not caused by any characteristic or specific change in systolic blood pressure.

The heart rate is elevated during attacks of angina pectoris induced by exertion. The elevation in heart rate under such conditions is undoubtedly a response of the heart to the degree and character of the work involved in the exercise. Attacks of angina induced by other stimuli are not necessarily accompanied by a change in heart rate. During the course of the present investigation an opportunity presented itself to measure the pulse rate in two individuals immediately before and within a few seconds after the onset of angina induced by sudden fright while the patients were at rest. In neither instance was the attack of pain accompanied by any appreciable change in pulse rate. Measurements of the blood pressure were not feasible, for the length of time necessary to adjust the blood pressure cuff would prevent observation of any transient changes. Mackenzie[23] has observed that the heart rate was increased in some patients during attacks while in others the rate became slower or was unchanged. Duke[11] has reported a case in which the attacks, precipitated by heat, were unaccompanied by any change in heart rate. Electrocardiograms taken by Levy,[20] Parkinson and Bedford,[24] and Brow and Holman[6] show the heart rate during

paroxysms of angina to be essentially the same as when the patient was free from pain, while the case reported by Gallavardin and Rougier[14] showed a distinct slowing during the attack. Feil and Siegel[13] have presented electrocardiographic tracings taken during attacks showing in some instances a definite increase in heart rate and in others an increase of less than 10 beats per minute. The tracings presented by Bousfield[4] show a similar slight increase in rate.

Wayne and Laplace[32] found a close correlation between the duration of attacks of angina induced by exertion and the length of time necessary for the heart rate to return to the resting rate. This was true in some of the cases included in the present study, but it was not true of all cases; in several instances the pain continued even after the heart rate had returned to the resting level.

Proger, Minnich, and Magendantz[26] noted that angina pectoris on exertion was associated in some patients with a failure of the heart rate to increase normally during exercise while in others extrasystoles developed shortly before the onset of pain. Similar reactions were noted in several of the patients studied in the present series. Since identical reactions were observed in patients without heart disease who did not develop pain on similar exertion and since angina pectoris was experienced by many patients who showed a normal cardiac response during exercise, these reactions in themselves cannot be held responsible for the attacks of pain.

The balance of evidence at the present time suggests that paroxysms of angina are induced by anoxemia or relative anoxemia of the heart muscle brought about by the inability of the coronary circulation to supply sufficient blood for the demands of the myocardium. The factors which influence the flow of blood through the coronary vessels are inadequately understood, but of undoubted importance are the caliber and rigidity of the vessels, the duration of systole and diastole, and the head of pressure at the mouths of the coronary arteries. Similarly, the demands of the myocardium are influenced by several factors including the frequency of contraction, the volume output, the velocity imparted to the blood stream, and the arterial pressure which the heart must maintain and work against.

Both the work of the heart and the coronary blood flow are influenced in part by the heart rate and the blood pressure. An increase in heart rate and systolic blood pressure increases the work which must be done by the heart, but at the same time these changes bring about an increase in coronary blood flow; whether the balance in a given instance enhances myocardial anoxemia or favors adequate myocardial nutrition cannot be prognosticated with certainty. Under certain conditions the rôle played by these two factors may be of major importance in causing a discrepancy between the supply and the demand. During episodes of paroxysmal rapid heart action, for example, the frequency and at times

irregularity of the cardiac contractions undoubtedly increase the energy expenditure of the heart muscle and at the same time probably decrease the flow of blood through the coronary vessels; it is not surprising that paroxysms of angina have been observed during such at-

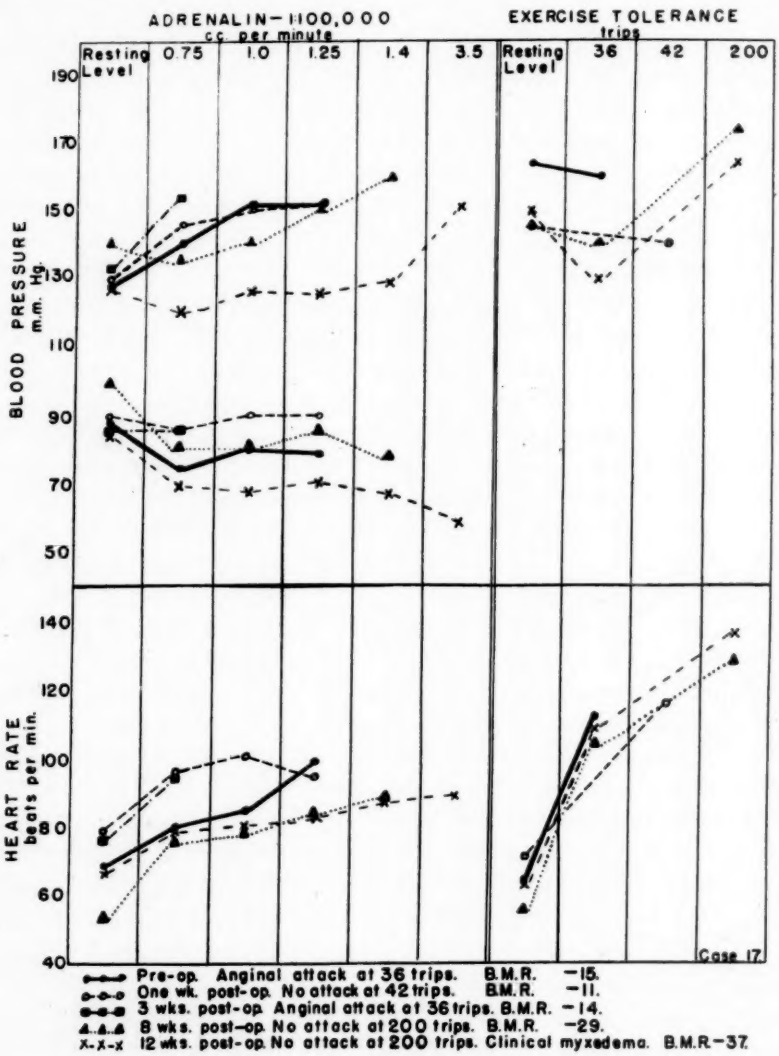

Fig. 5.—Response of the heart rate and blood pressure to exercise and to intravenously injected adrenalin both before operation and after total thyroidectomy when various degrees of clinical improvement were evident.

tacks.[7, 34, 35] Similarly an increase in heart rate and systolic blood pressure in a patient with aortic regurgitation is likely to be accompanied by heart pain, for the low diastolic pressure prevents adequate filling of the coronary vessels. These situations, however, are unusual in the majority of attacks which occur clinically; other factors, such as the

inadequate flow of blood through rigid or spastic coronary vessels and the increased requirements of the heart during exercise, are of major importance.

The clinical improvement, in patients with chronic congestive failure or angina pectoris, following total thyroidectomy, is apparently independent of changes in sensitivity to adrenalin or changes in the amount of adrenalin secreted by the body. It has been suggested that a change in sensitivity to adrenalin[5, 10, 12] or a decreased response of the heart to stimuli such as adrenalin or exercise[30] is responsible for the clinical improvement which follows total thyroidectomy.

In a previous investigation[28] the sensitivity to adrenalin was measured by studying the changes in blood pressure, heart rate, respiration, and oxygen consumption produced in man by known doses of adrenalin administered continuously by the intravenous route. The sensitivity to adrenalin measured by these criteria was the same before operation and after total thyroidectomy when clinical improvement was manifest. (Fig. 5.)

Although there was no change in sensitivity to adrenalin at the levels of hypometabolism maintained in these patients following total thyroidectomy, it is conceivable that the secretion of adrenalin is diminished, and the heart, therefore, is subjected to less intense stimuli.[28]

Unfortunately, quantitative tests for the determination of circulating adrenalin in man are not available. Indirect evidence regarding the concentration of circulating adrenalin can be obtained by measuring changes in heart rate and blood pressure, for tachycardia and an increase in arterial tension are characteristic physiological responses to adrenalin. If secreted adrenalin plays any part in the heart rate and systolic blood pressure changes during exertion, a diminution in adrenalin output following thyroidectomy would be evidenced by relatively less change in heart rate and systolic blood pressure during exercise. This is not the case, for during the prolonged exertion made possible by total thyroidectomy the heart rate and systolic blood pressure rise as high as, or higher than, during exercise before operation (Table III and Figs. 4 and 5).

There is, therefore, no evidence that exercise calls forth either a diminished secretion of adrenalin or a diminished response of the heart rate or blood pressure in man after total thyroidectomy. The improvement is rather to be related to a more favorable readjustment between diminished demands of the myocardium[2] and the available supply of blood through the coronary vessels.

SUMMARY

Attacks of angina pectoris were induced in thirty-five patients by exercise under standardized conditions. The systolic blood pressure and heart rate were determined at half-minute intervals during and follow-

ing such exercise. In this manner it was possible to determine the systolic blood pressure and heart rate not only during attacks of angina pectoris but also immediately before and at the very onset of the paroxysms of pain.

The systolic blood pressure at the onset of such attacks was higher in some cases, lower in others, and in many instances essentially the same as the blood pressure during rest. Measurements made shortly after the cessation of exercise, while the pain still persisted, revealed the systolic blood pressure to be higher than the resting level in most instances. These variations in blood pressure were the result of two factors: (1) the changes in blood pressure brought about by exercise and (2) the duration of the exercise before being terminated by the onset of pain.

The heart rate at the onset of the attacks was invariably increased; the degree of increase varied with the duration of exercise required to induce the attack and the curve of increase of the heart rate during exertion. Measurements made shortly after the cessation of exertion, while the pain still persisted, revealed the heart rate to be elevated but to a significantly lesser degree than at the onset of the attack.

Similar changes in systolic blood pressure and heart rate during and after exercise were observed in patients without evidence of heart disease.

Observations were made in patients before and after total ablation of the thyroid gland. With the prolonged exertion made possible by this operation, the systolic blood pressure and heart rate rose as high as or higher than it did during exercise before operation.

The wide variation in systolic blood pressure and heart rate at the onset of attacks of angina indicates that such changes are not primary etiological factors in their precipitation and are of no value in diagnosis.

There was no evidence that the clinical improvement following total thyroidectomy was due to a lessened increase in heart rate or systolic blood pressure or to a decreased output of adrenalin during exertion.

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LIGATION OF THE CORONARY ARTERIES IN JAVANESE MONKEYS*

II. Arrhythmias and Conduction Disturbances

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IN PART I[1] we described the changes in the ventricular electrogram which supervened after ligation of the ramus descendens anterior (L) in seventeen monkeys (*Macaca irus*) and of the right artery (R) in fourteen of these animals. In one monkey the right artery was obstructed seven weeks after left ligation.

The following discussion concerns the arrhythmias which were observed in these monkeys, whether they were accompanied by conduction disturbances or not. They include extrasystoles, paroxysmal tachycardia, ventricular fibrillation, sino-auricular block, auriculoventricular block, bundle-branch block, and nodal rhythm.

It should be noted at once that no case of flutter or fibrillation of the auricles was observed. It is possible that this is due to the fact that the arteries were ligated too far from the aorta to include with certainty any possibly existing rami cristae terminales or rami atriales. Lesions of the auricles were not found morphologically.

EXTRASYSTOLES

To localize the point of origin of ectopic beats by means of the electrocardiogram, the only method available, in our experience it is necessary to make simultaneous records of at least two and preferably all three of the standard leads. It can happen, for instance, that in Lead I a ventricular complex is seen without any preceding P-wave, while in Leads II and III P-waves, both negative and of the same size, prove to be present (See Fig. 1, segment B). If recording had been made successively and not simultaneously, the latter complexes would probably have been assigned to another point of origin.

Moreover, in successive registration it is never known with certainty whether the extrasystoles caught in the different leads really represent the same type—in other words, whether they had a common point of origin.

For such reasons we have, especially when studying extrasystoles, always had great success with the use of simultaneous recording and have met with difficulties whenever the records were made successively.

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An experimental study made by one of us,* which was begun at about the time we started the coronary ligations and will be published separately, put in our hands the various types of electrocardiogram appearing in the three simultaneous leads when the Macaca heart is stimulated by induction shocks at various places, the thorax being closed, the animal respiring spontaneously. On the basis of these results, which in general agree with those recently published by Kountz and his associates,[2] we were usually able to determine from our curves the point of origin of the extrasystoles observed in our coronary monkeys.

First and foremost let it be emphasized that we never found any irregularity in the heart action of monkeys before operation. In the past years we have examined over 300 monkeys and have never found one with a spontaneous extrasystole. Our experience is that these "spontaneous" extrasystoles in various experimental animals, and certainly in monkeys,

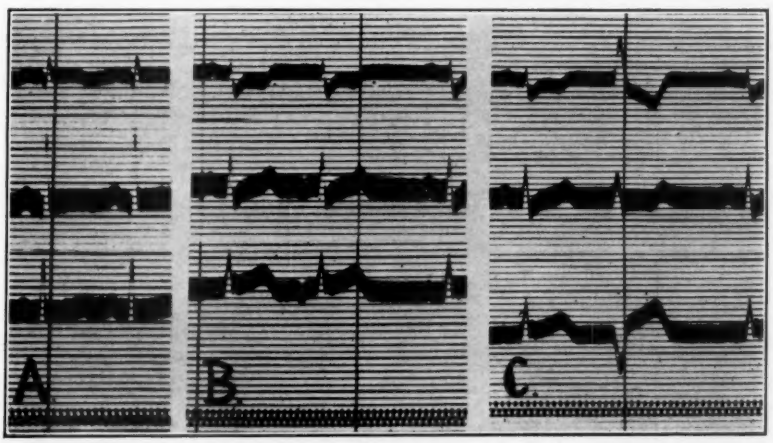

Fig. 1.—Monkey 37 R. *A*, before operation; *B*, 15 min., *C*, 17 min. after ligation of right artery. Second complex in *B* shows auricular extrasystole without P in Lead I, but with negative P in Leads II and III. Second complex in *C* ventricular extrasystole from right apex, interfering with P-wave.

occur less frequently than in man, which is perhaps of some interest to the clinician. Nor did we ever see extrasystoles develop in a monkey under the influence of "emotion" or under the influence of the narcosis as applied in our experiments.[3] We are convinced, therefore, that the extrasystoles described here may be regarded as resulting from the coronary ligations.

They may, then, be unspecific (i.e., due to the operative trauma as such), or specific (i.e., due to the changes produced in the heart by the coronary obstruction as such), formerly called by Lewis[4] a local state of irritability in the area of the anemic heart wall.

First, as regards the influence of the operative trauma, which as a rule is not considered of importance:[5-7] it is our experience that extensive operations in the monkey thorax (for instance, the entire operation already described without coronary ligation but including the passage of

*Storm.

a ligature through the superficial layers of the heart muscle, or the exposure of the heart and subsequent incision and section of parts of the conduction system) usually may be done without inducing extrasystoles. Also such operations are in our experience not followed by ectopic beats. Since about 60 per cent of our monkeys after coronary ligation showed no extrasystoles, it is our opinion that no great etiological significance need be attached to possible mechanical irritation by the ligature itself. Moreover, it might be expected that any postoperative extrasystoles which did arise as a result of such direct irritation would originate at the site of the ligature. To what extent such extrasystoles probably ap-

TABLE I

NUMBER AND TYPE OF EXTRASYSTOLES OBSERVED AFTER LIGATION

MONKEY	FIRST E. S. OBSERVED AFTER LIGATION	LAST E. S. OBSERVED AFTER LIGATION	SURVIVAL AFTER OPERATION	NUMBER AND TYPE OF E. S.
4 L	48 min.	63 min.	6 mo.	1 nodal 5 base* 7 left* 1 right*
5 L	20 min.	20 min.	36 min.	1 nodal 1 left*
6 L	1 wk.	1 wk.	7 wk.	1 apex*
6 L + R	65 min.	65 min.	4 hr.	3 auricular
13 L	10 min.	10 min.	23 min.	1 left apex
16 L	7 min.	7 min.	13 min.	1 nodal or apex†
19 L	4 days	4 days	2 mo.	1 base*
10 R	5 hr.	3 mo.	6 mo.	336 right apex and 48 left apex
12 R	1 day	12 days	5½ mo.	313 right apex and middle
14 R	4 min.	8 min.	4 mo.	2 right base
36 R	22 min.	22 min.	6 hr.	3 right apex
37 R	15 min.	18 min.	1 hr.	1 auricular and 1 right apex

*Not to be localized more exactly because seen in only one lead.
†Not to be localized more exactly because complicated by bundle-branch block.

peared in our experiments will be discussed after we have first presented in Tables I and II a review of the extrasystoles recorded after coronary ligation.

Records were made several times per hour in the first two or three hours after the operation, the projection of the strings being carefully watched in the intervals. When the monkey survived for a longer period, curves were taken about twice a week. Each record contained about 20 cardiac cycles in each lead, taken simultaneously or successively. It was, of course, practically impossible to leave the animals continually connected to the galvanometers. It is certain, therefore, that although about 1,200 curves were made, there have been more extrasystoles among our material than could be collected for our tables.

Some of the curves with extrasystoles after ligation are reproduced in this paper; one was shown in Fig. 14, Part I.

TABLE II

RELATION BETWEEN TYPE OF EXTRASYSTOLE AND TYPE OF LIGATION

	LEFT LIGATION	RIGHT LIGATION
Total number of monkeys	17	15
Total number showing extrasystoles	6	6
Among these showed:		
Auricular E. S.	0	2
Nodal E. S.	2	0
Left ventricular E. S.	3	1
Right ventricular E. S.	1	5
Left base E. S.	0	0
Left apex E. S.	1	1
Right base E. S.	0	1
Right apex E. S.	0	4
Undetermined	5	0

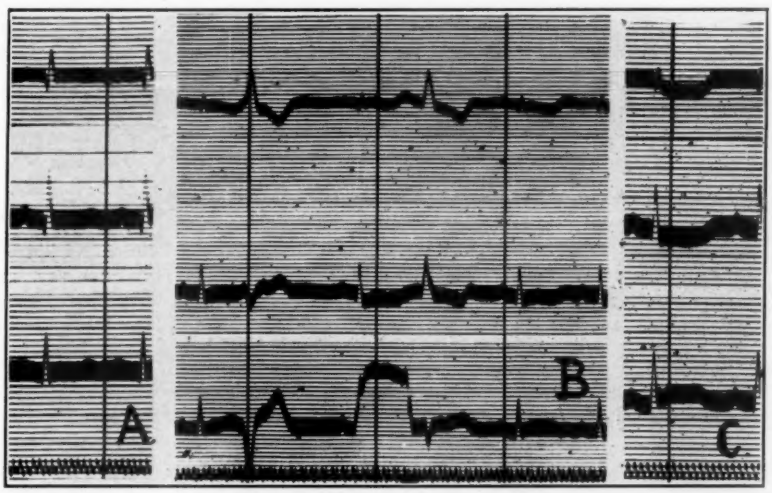

Fig. 2.—Monkey 36 R. *A*, before operation; *B*, 22 min., *C*, 52 min. after ligation of right artery. In *B* second complex extrasystole from right ventricular apex, fourth complex point of origin a little higher, but still in apical part. In *B* Lead III calibration deflection just before second extrasystole.

In spite of the fact mentioned above, that we do not attribute any dominant significance to local irritation caused by the ligature and practically none to operative trauma, we will not entirely exclude the former as a possible cause of a part of our extrasystoles. We regard such local irritation as a possible cause of the nodal and basal extrasystoles of Monkeys 4 L, 5 L, and 14 R, for they all originated in or near the place of ligation, appeared shortly after the operation, and were not seen again in subsequent records. The same holds good for the auricular extrasystole of Monkey 37 R (Fig. 1 *B*), in which animal the ligature was found by microscopic examination to have included also a small part of the right auricle.

On the other hand, we are of the opinion that the extrasystoles originating in the apical part of the ventricles (as in Fig. 2) could not arise

from local irritation of the ligatures and must therefore be regarded as specific results of the internal changes developed in or near the muscle area formerly supplied by the ligated vessel.

In particular, Monkeys 10 R and 12 R point to the possibility that such extrasystoles, especially if they show a tendency to persist for a

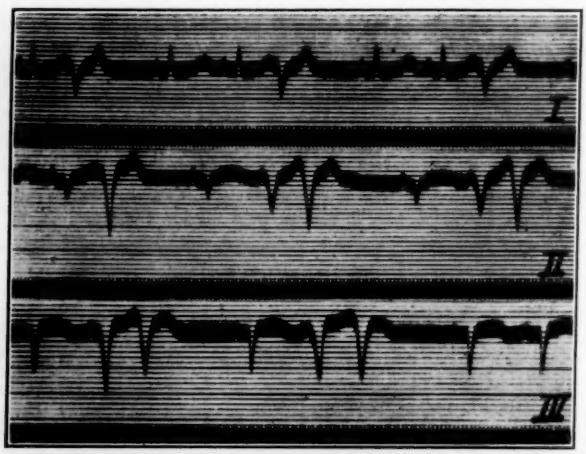

Fig. 3.—Monkey 10 R. Isolated and coupled extrasystoles, originating in left apex, six days after ligation of right artery. This was seen only once in this animal; the other extrasystoles preceding and following the paroxysm were of the right apex type. See also Fig. 5 *A*.

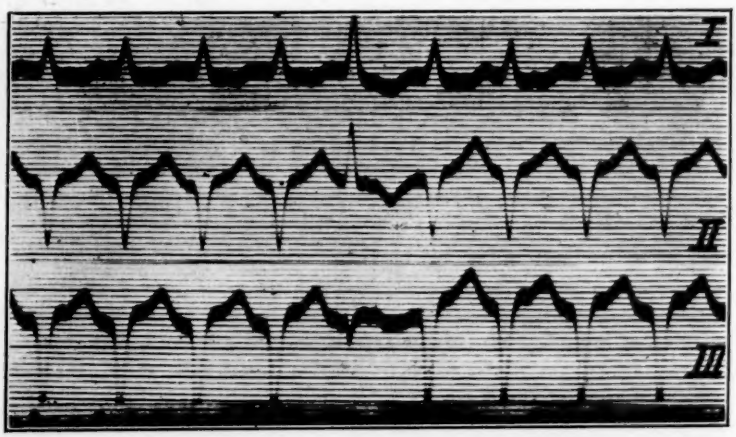

Fig. 4.—Monkey 10 R. Paroxysm of ventricular tachycardia, one week after ligation of right artery, originating in right apex, the fifth complex in right apex somewhat higher.

long time and to develop into paroxysms of ventricular tachycardia, can bear a more or less localizing character.

Repeating this investigation with a larger number of monkeys and with still more frequent electrocardiographic recordings would probably place this opinion, which is also found in the literature,[8-14] on a more certain basis.

PAROXYSMAL TACHYCARDIA

In Monkeys 10 R and 12 R we observed salvos of extrasystoles, starting and ending as isolated or coupled ectopic ventricular beats of the same type as seen in the paroxysm.

The increase in heart rate during these attacks is in monkeys not as large as in man. This is undoubtedly connected with the fact that the normal monkey heart beats so rapidly that the normal diastole is shorter than the normal systole.[3]

Monkey 10 R.—The type of extrasystole before the paroxysms usually indicated the right apex as the point of origin, with this remarkable exception that on a given day (Fig. 3) groups of one or two extrasystoles were observed originating in the left apex.

The paroxysms on the following days (Fig. 4) and also all extrasystoles thereafter were, however, clearly of the right apex type. In connection with the septum

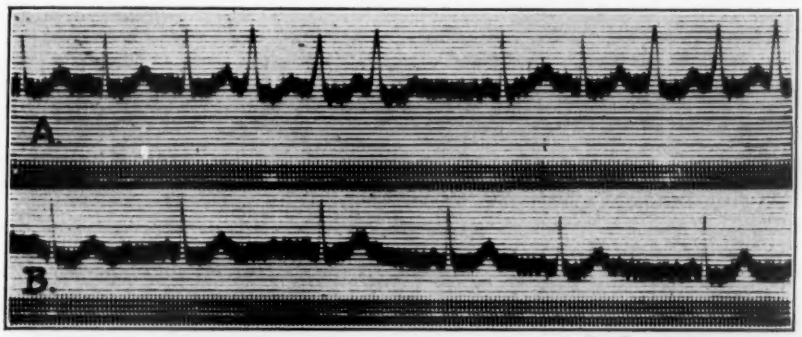

Fig. 5.—Monkey 10 R. Eight days after ligation of right artery. Lead I only. *A*, before; *B*, during bilateral pressure on region carotid sinus. Vagus reflex.

lesion, described in this animal, this temporary variability of extrasystole type appears to us in all probability to indicate a point of origin that usually was located in the right apical part of the septum but occasionally and exceptionally lay in the contiguous left apical part.

This monkey showed beforehand (Fig. 10) a prolonged P-R interval, periods of Wenckebach, and dropped beats.

A remarkable observation was made in this animal on April 28, 1933, when we succeeded, as shown in Fig. 5, eight days after the operation, in temporarily checking the paroxysm by a bilateral pressure on the region of the carotid sinus, comparable to the clinical "vagus pressure test," which in fact concerns a vagus reflex. That we were dealing here with such a reflex, as described by Hering,[15] and not with a casual change in the rhythm, was proved in our opinion by the fact that the frequency of the normal heartbeats, which was 180 in the intervals between the paroxysms, fell to 96 during pressure on the carotid sinus (Fig. 5 *A* and *B*). At the same time the P-R interval was shortened, indicating

probably a downward shifting of the pacemaker. Immediately the pressure was released, the paroxysms of extrasystoles returned, for a time even more violently (in groups of six or seven as against the earlier groups of three). After that day no further attacks were observed although now and then there appeared isolated extrasystoles of the right apex type; thus at the time the extrasystoles reacted to the "vagus pressure," they were already in all probability tending to disappear from other causes. Still our observation in this monkey seems conformable to those of Lewis[8] in the dog, in which animal paroxysms could be checked by electrical vagus stimulation in 30 per cent of his cases.

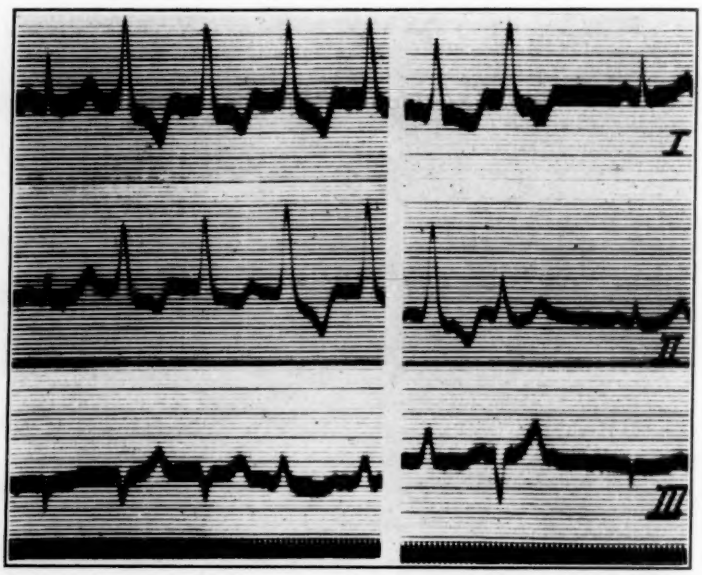

Fig. 6.—Monkey 12 R. Beginning and end of paroxysm of ventricular tachycardia, originating principally in right apex, but sometimes somewhat higher, 9 days after ligation of right artery.

Monkey 12 R showed no septum lesions. One day after the right ligation isolated extrasystoles of the right apex and right middle type appeared (Part I, Fig. 14 *C*), which increased to paroxysms some days later (see Fig. 6). These remained for one day only and disappeared in the course of the next four days, passing through a stage of isolated extrasystoles. If a study had been made only in Lead I, it would have been impossible in the case shown in Fig. 6 to detect the migration of the point of origin from the apex to the middle of the right ventricle and vice versa (see especially Lead III).

One would be tempted to connect the appearance of an extrasystole of other type at the end of a paroxysm (see Fig. 6) with the ending of the attack as a matter of cause and effect since it seems possible experimentally to end a paroxysm by interjecting a second circulating wave into one that is already established.[16] However, we observed in clinical curves as well as in our experimental ones that similar extrasystoles of

other type often do not bring such a paroxysm to an end (see Fig. 4) and, on the other hand, that quite often an attack ends without the intervention of an extrasystole of other type.

Paroxysms of ventricular extrasystoles were seen only in the two monkeys described above, in both cases after ligation of the right artery. In cats and dogs they seem to occur more frequently, also especially after right ligation.[8, 10, 11] Why, then, were they relatively so uncommon in our monkeys? Perhaps in this regard the following is of some importance.

The monkey heart is probably only accessible to ectopic stimuli for a very short time, owing to its relatively long systole and relatively very short diastole. A larger portion of these stimuli will threaten to occur during systole and at that period will be either incapable of producing

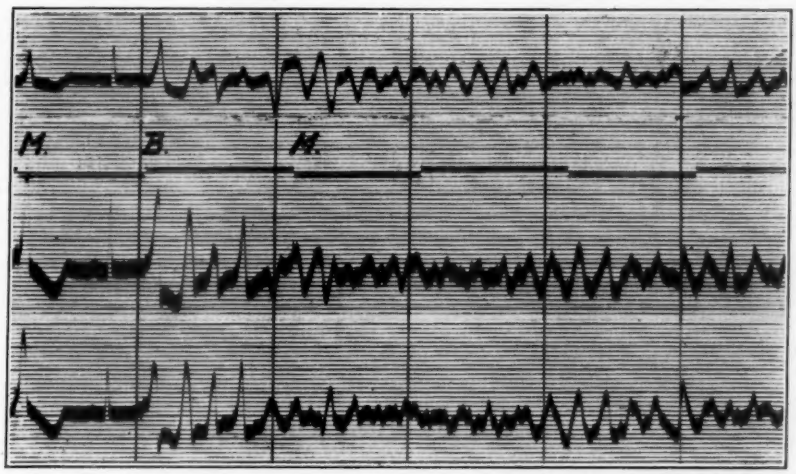

Fig. 7.—Ventricular fibrillation in Macaca after stimulating conus arteriosus with break shock (*B*) at end of systole. Thorax closed. Spontaneous respiration. First complex: extrasystole from conus arteriosus; second: last normal electrocardiogram during which the fatal stimulus *B* enters.

any effect or, if falling toward the end of systole, will tend to produce fibrillation.[17, 18] Thus the monkey heart might have a smaller chance to develop extrasystoles or paroxysms during a longer period and a greater chance to fall soon into fibrillation.

Thinking along these lines we come automatically to the study of ventricular fibrillation in our monkeys.

VENTRICULAR FIBRILLATION

In the course of his investigations of experimental extrasystoles mentioned above, one of us* was able to record that actually in Macaca a ventricular extrasystole, provoked artificially in the latest part of a normal systole, can pass over into fibrillation (see Fig. 7).

*Storm.

This is in accordance with the observations in frogs and dogs which have just been mentioned[17, 18] and also with a record Feil and his associates[19] made in a dog after coronary ligation.

It is therefore possible that in those of our monkeys which developed ventricular fibrillation the cause lay in one or more extrasystoles occurring just at the "fatal" moment. We did not succeed, however, in photographing this, nor could it be deduced with certainty from the observations collected in Table III.

TABLE III

REVIEW OF EXTRASYSTOLES OBSERVED IN THOSE MONKEYS WHICH DEVELOPED VENTRICULAR FIBRILLATION

MONKEY	TIME OF APPEARANCE OF VENTRICULAR FIBRILLATION AFTER OPERATION	PRECEDING EXTRASYSTOLES OBSERVED OR NOT	REMARKS
5 L	36 min.	Yes	
13 L	23 min.	Yes	
15 L	33 min.	No	
16 L	13 min.	Yes	
19 L	±2 mo.	Yes	Small amount of chloroform.
26 L	27 min.	No	
49 L	5 days	No	
52 L	16 min.	No	
40 R	35 min.	No	
X R	15 min.	No	Both vagus nerves previously cut.

However, in regard to Table III, it must be noticed that: (a) we never succeeded in recording the beginning of fibrillation in these monkeys, and therefore it is possible that the "fatal" extrasystole escaped us; (b) there may have been isolated extrasystoles which, in spite of our numerous recordings, also escaped us; (c) it is possible that still more monkeys died of fibrillation, as will be described later.

Nevertheless, it is certainly remarkable that just the monkeys which showed the most extrasystoles (10 R and 12 R) did not pass into fibrillation, and further that the frequency of the phenomenon seemed much greater after left ligation than after right ligation, a fact which was not observed of the extrasystoles. Of the twelve monkeys which showed extrasystoles, six after left and six after right ligation (see Tables I and II), only four, all left monkeys, went with certainty into fibrillation.

To what extent is the fibrillation we have described specifically the result of the disturbance in the coronary circulation; to what extent is it not?[20]

Fibrillation can for instance be caused by a mechanical stimulus falling at a "fatal" moment in the cardiac cycle, but in that case it begins immediately. We did observe this kind of fibrillation in cases of bundle-branch sections at the instant the knife cut into the ventricle, or in experiments on extrasystoles at the instant electrodes were stuck into the

heart muscle. We observed it also in Monkey 28, which was not further discussed here, in which it started at the very first attempt to ligate the left artery at the very first prick of the needle before anything was tied off. This immediate beginning is characteristic of mechanical fibrillation.

In the cases of Table III, which shows that in eight out of seventeen left monkeys and two out of fifteen right monkeys the heart went with certainty into fibrillation, in our opinion this "mechanical" fibrillation did not play any part.

Was the fibrillation caused by the narcosis or by the operative trauma?

In the course of many thoracotomies on monkeys we have never observed a case of fibrillation as long as the heart was not operated on, nor did we ever see a case induced by pernocton or evipan sodium narcosis per se. Neither the operative trauma as such nor the narcosis as such need therefore be taken into consideration here as etiological factors.

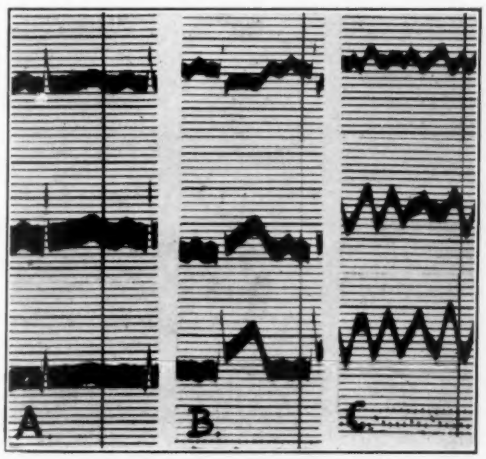

Fig. 8.—Monkey X R. *A*, before operation; *B*, 10 min., *C*, 15 min. after cutting both vagus nerves and ligation of right artery.

For these reasons we regard the cases of fibrillation collected in Table III as a sequel of local biological changes in the heart caused by the disturbance in the coronary circulation. In this connection it must be pointed out, however, that certainly in Monkey 19 L and probably in Monkey X R a secondary cause also played a part.

In *Monkey 19 L* two months after the operation, when the animal became restless during a registration, a very small amount of chloroform was administered by an assistant, something which had never been done before and has never been done since in our series of experiments. Fibrillation set in immediately.

In *Monkey X R* the vagi were cut on both sides before the ligation in order to observe if this procedure would affect the S-T deviation expected or would promote the appearance of extrasystoles. No noticeable influence upon the S-T deviation was found, but it is possible[12] that the development of fibrillation was thereby accelerated (see Fig. 8).

We have described as fibrillation only those cases which could with certainty be recognized as such, either by actually seeing the heart fibrillating or by the electrocardiographic record or by noticing the typical vibrations of the string. It is, however, not excluded that also Monkeys 17 L, 23 R, 36 R, and 41 R died in fibrillation, two days, six hours, six hours, and four days, respectively, after their operations. Among these animals only 36 R showed extrasystoles. It is true that we did not observe their fibrillation as such. In Monkey 6 L + R we believe fibrillation improbable. In Monkeys 25 R and 37 R we know for certain that the heart finally stopped beating without intervening fibrillation. These last monkeys showed a fading of the heart action, an increasing bradycardia with bizarre terminal ventricular complexes, similar to those seen in suffocation. It is probable that in these cases a primary heart insufficiency caused a failure of respiration and this finally a secondary failure of the heart due to asphyxia.[21]

Not only in experimental suffocation of Macaca, but also after the very rapid intravenous injection of large doses of pernocton or evipan sodium, which we usually give for killing an animal instantaneously, the heart stopped according to electrocardiographic control quite certainly without any fibrillation.

From the described observations on fibrillation we conclude that the chance of fibrillation after coronary ligation is relatively greatest during the first forty minutes; that if it has not developed within about five days, there is a very great probability that it will never set in; and finally that quite certainly not every death after coronary ligation is to be attributed to fibrillation.

Fibrillation once developed, or at least once observed, never stopped spontaneously. Nor could we ever succeed in stopping fibrillation by chemical or physical methods, as, for instance, described by Wiggers[22] and Hooker.[23] Without going into the theories of fibrillation, let us state that these measures did not prove effective in cases of fibrillation after coronary ligation.

CONDUCTION DISTURBANCES

In the experimental animals, discussed below, various conduction disturbances were observed. The origin of these disturbances must be sought in the coronary obstruction since they never appeared in monkeys to which the same methods of narcosis and operation were applied, but the coronary artery was not ligated.

Monkey 16 L.—One or two minutes after ligation of the anterior descending branch, an S-T deviation appeared. In this animal the leads were recorded only successively. After five minutes, while Lead I was actually being recorded (Fig. 9 *C I*) there appeared a disturbance of intraventricular conduction. This disturbance was characterized in Lead I by a progressively increasing downward S-wave and upward T-wave (complexes *b*) and began originally alternating with the earlier developed "normal" coronary electrocardiogram (complexes *e*). There later appeared (partly reproduced) two groups of five complexes (*b*) separated by one

complex (*e*) after which *b* became permanent; and also Leads II and III, taken in succession, proved permanently inverted (*C II* and *C III*); in both Leads II and III QRS is inverted and broadened, while in Lead III it is also clearly feathered. In both, the after-wave is high and positive.

What here develops within one minute (five minutes after ligation) can hardly be anything other than a *bundle-branch block* in this monkey, presumably a right block. It is, however, quite possible that the right block caused by section of the bundle branch in a normal monkey heart shows another form of curve, since in our case the coronary ligation might have changed the function of the ventricular muscle also peripherally to the conduction system.

Finally an extrasystole (*D II*) was seen in this animal, which thirteen minutes after the ligation developed ventricular fibrillation. This extrasystole was unfortunately observed only in Lead II. Therefore the point of origin cannot be

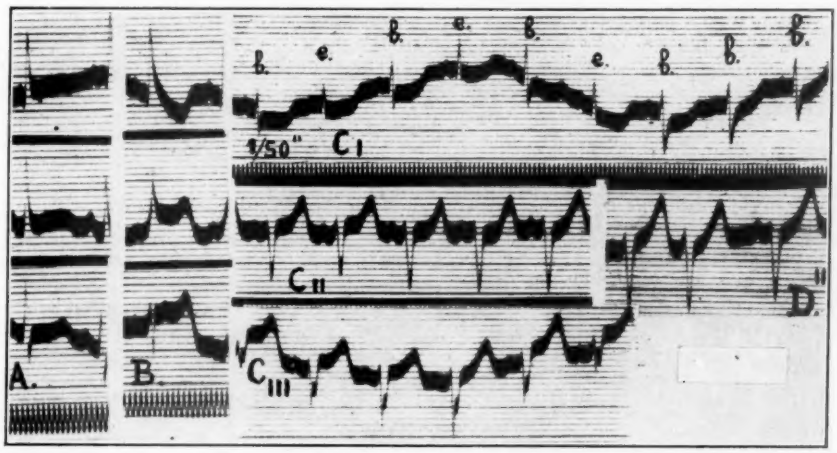

Fig. 9.—Monkey 16 L. Leads taken successively. *A*, before operation; *B*, 2 min., *C*, 5 min., *D*, (Lead II only) 7 min. after ligation of the ramus descendens anterior. In *C*, during Lead I development of bundle-branch block (*b*), at first alternating with normal beats (*e*), later consecutive. Fully developed in *C II* and *III*. In *D II* second complex extrasystole. Further details in text.

determined exactly, especially since the ventricular electrocardiogram has already been modified by the bundle-branch block. Was it a nodal extrasystole forced into recording an abnormal ventricular complex, or did it originate in the left or right ventricular apex, in both cases recording such a complex in a normal heart? In this instance Lead I, which is at present lacking, would have been especially useful for giving further information. It may be concluded from the curves that in this monkey very probably the septum function was disturbed although, as a result of the short survival of the animal, a lesion did not become manifest. We shall discuss later this septum involvement in connection with the direction of the S-T axis here observed (+99°).

Monkey 10 R.—After right ligation a definite S-T deviation appeared within about two minutes. The P-R interval before the operation was 0.07 sec. (normal in a monkey); eight minutes after the operation it was 0.10 sec.; twenty-eight minutes after the operation Wenckebach's periods and dropped beats appeared (Fig. 10)

during which P-R increased to 0.13 sec.; one hour after the ligation P-R was 0.12 sec. and the symptom of dropped beats had disappeared. This increase of the P-R interval remained for about five days, after which P-R again returned to 0.07 just

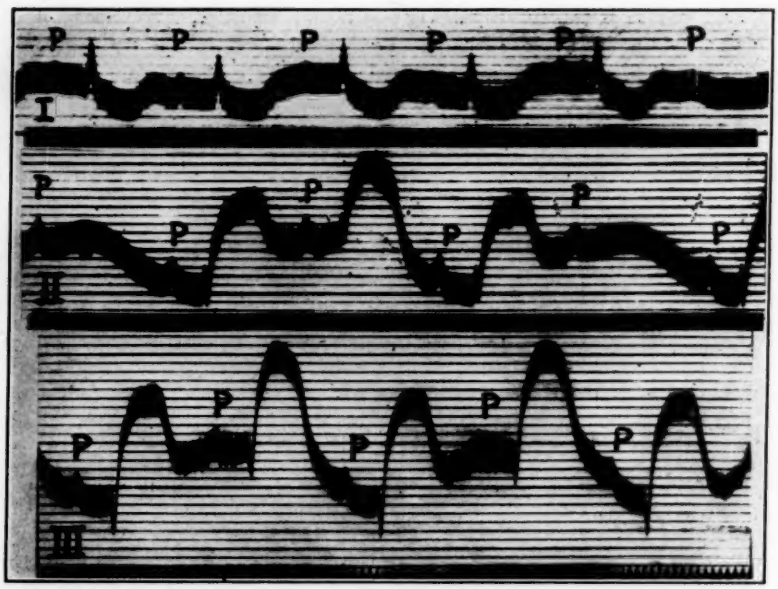

Fig. 10.—Monkey 10 R. Leads taken successively, 28 min. after ligation of right artery. Progressive lengthening of P-R interval, dropped beats. See also Part I, Fig. 7 and this paper Figs. 3, 4, and 5.

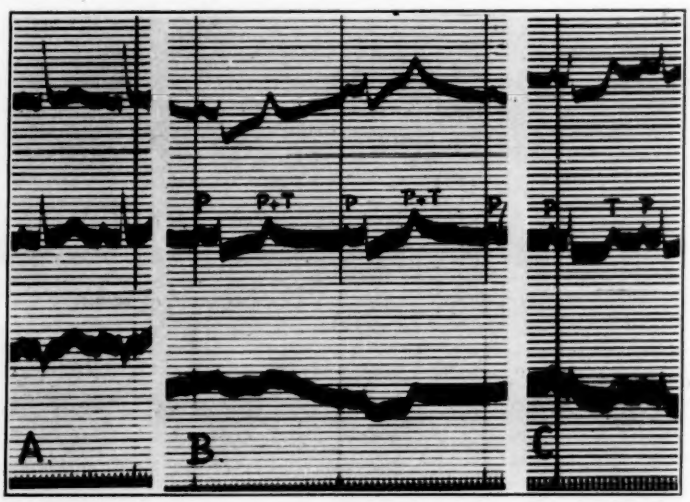

Fig. 11.—Monkey 25 R. *A*, before operation; *B*, 4 min., *C*, 9 min. after ligation of right artery. During *B*, 2 to 1 block.

about at the time the attacks of ventricular extrasystoles (see above) began to appear.

Monkey 25 R.—After ligation of the right artery a definite S-T deviation developed within about four minutes. Before the operation the P-R interval was 0.07 sec.

and the ventricular rate 225 per minute. Four minutes after the operation a 2 to 1 block set in with a sometimes slightly shortened P-R interval and a ventricular rate of 120 (see Fig. 11). It appears that the auriculoventricular node or bundle was still conducting quite well at this frequency of 120 per minute but that it became very easily fatigued or recovered slowly and therefore could not pass the 240 sinus

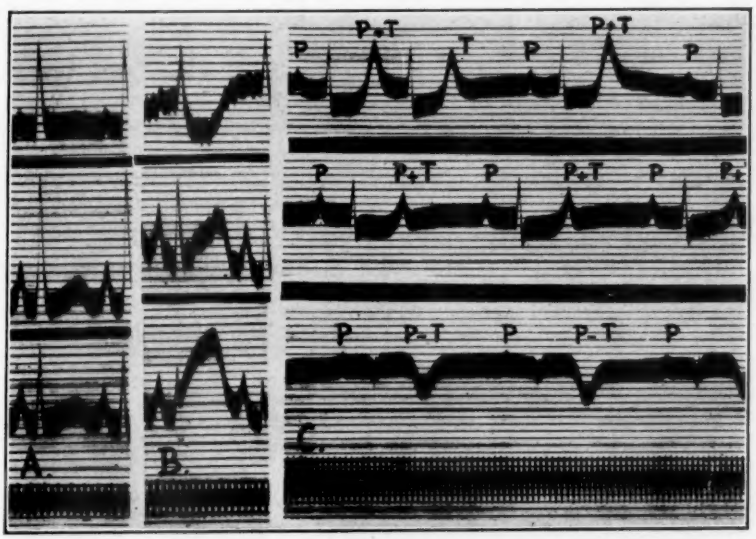

Fig. 12.—Monkey 6 L+R. *A*, before operation; *B*, 34 min. after ligation of the ramus descendens anterior on March 28, 1933. *C*, 1 hour after ligation of right artery on May 17, 1933. In *C*, 2 to 1 and 3 to 2 block, lengthened P-R interval. During Lead I sometimes sino-auricular block.

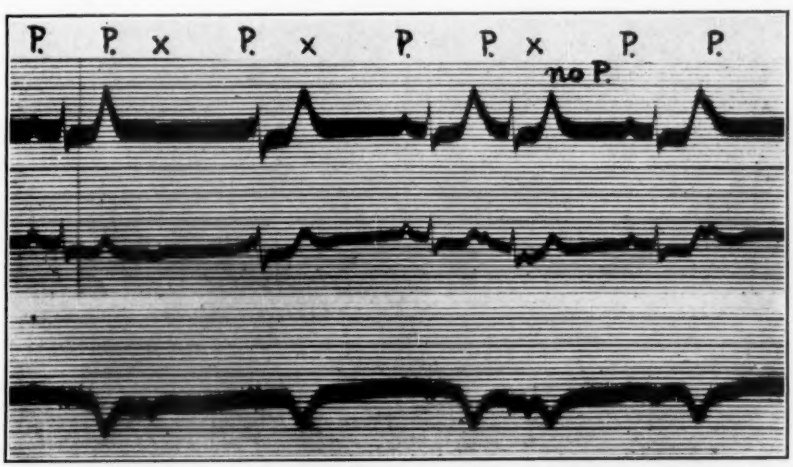

Fig. 13.—Monkey 6 L+R. Taken 65 min. after ligation of right artery. At *X* auricular extrasystoles (showing in Leads II and III a negative P-wave), not passing to the ventricle, but followed by compensatory pause in P rhythm. Second ventricular complex represents escaped nodal beat. Note 3 to 2 and 2 to 1 A-V block. See also text.

impulses per minute. This 2 to 1 block, however, existed only for about one minute and did not recur. The P-R interval returned to 0.07 sec. and the ventricular rate to about 200. The animal died in about one hour without fibrillation (see above).

Monkey 6 L + R.—After ligation of the anterior descending branch an S-T axis developed, as already described, in the mixed field (+127°). Before operation the heart rate was 245, the P-R interval 0.07 sec., and the length of ventricular systole 0.15 sec. These did not change after the left ligation (Fig. 12 *B*). After seven weeks the right coronary artery was ligated. Again there appeared an S-T deviation (−160°, right field) and a definite secondary coronary electrocardiogram developed with prolongation of the ventricular systole to 0.23 sec. and an interval from the beginning of QRS to the summit of the after-wave of 0.15 sec., being exactly the original length of systole. At first there appeared a 2 to 1 block in which the minimum P-R interval was 0.11 sec., the sinus frequency 202, and the ventricular rate 101. Afterward a remarkable rhythm was discovered (Fig. 12 *C* and Fig. 13). We noticed sometimes a 2 to 1 and sometimes a 3 to 2 block (dropped beats with Wenckebach's periods), further a temporary 3 to 2 sino-auricular block, and auricular extrasystoles not passing over to the ventricle, but followed by a compensatory pause in the P rhythm. Occasionally there were also escaped nodal beats.

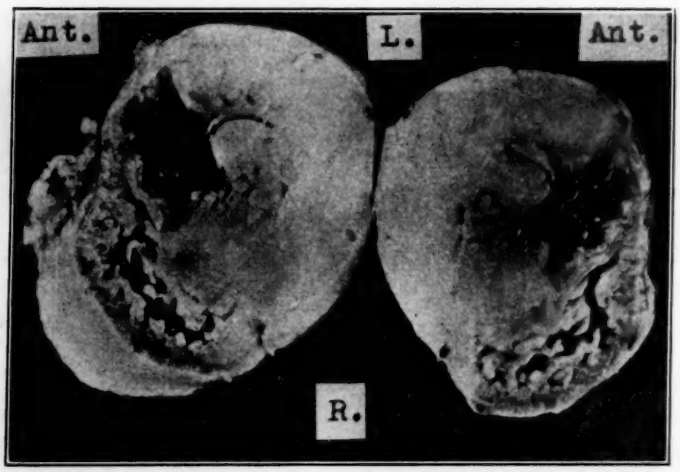

Fig. 14.—Heart of Monkey 6 L + R. Lesion of left ventricular wall and anterior part of septum caused by the first ligation (ramus descendens anterior), which occurred seven weeks previously.

Perhaps in this monkey the auriculoventricular bundle or node became either less conductive or sooner fatigued; it is also possible that the ventricle in lengthening its systole lengthened also its refractory period and thus contributed to the arrhythmia. The blocked auricular extrasystoles point in our opinion to a disturbance of the auriculonodal regions. This animal died some hours after the second ligation, apparently from circulatory failure. There were no indications of fibrillation. The heart clearly showed the result of the left ligation (Fig. 14).

In one case, after ligation of the right coronary artery close to the aorta, the function of the higher pacemaker was obviously practically eliminated, with the consequent gradual development of a slow nodal rhythm.

Monkey 23 R.—Within two minutes after ligation of the right artery the S-T deviation was seen, described in Part I, accompanied by after-waves in the opposite direction and prolongation of the ventricular systole from 0.19 to 0.26 sec. After 20 minutes a downward shifting of the pacemaker began; P_1 decreased, P_2 became diphasic, and P_3 negative, all gradually approached R and finally appeared directly in

contact with the ventricular complex (Fig. 15 *D*), so that the negative P_2, if studied only superficially, might erroneously be taken for a Q_3-wave. At the same time the heart rate decreased because of the lower frequency of the shifted pacemaker. This heart rate before operation was 171, four minutes after operation 158, twenty minutes after operation 113, and seventy-three minutes after operation 120 per minute.

We have already pointed out in Part I (Cases 23 *A* and 23 *B*) that, while the S-T deviations in Leads I and III (which were in opposite directions) increased, the S-T segment in Lead II tended to become isoelectric (Fig. 15 *B* and *D*). This meant a rotation of the S-T axis of only 10°. Lead II, considered by itself, if no notice be taken of the nodal rhythm, showed a "normal" electrocardiogram, which is once more a warning never to be satisfied with the results of a single lead. Since the after-waves in Leads I and III practically neutralize one another, the prolongation of systole does not become manifest in Lead II, as was also described in Part I. In

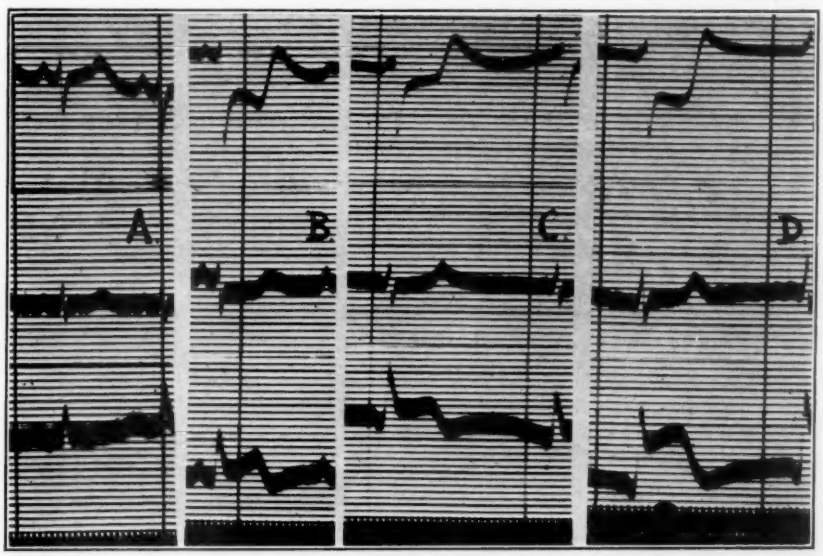

Fig. 15.—Monkey 23 R. *A*, before operation; *B*, 3 min., *C*, 20 min., *D*, 73 min. after ligation of right artery. Nodal rhythm develops. Little change in the ventricular complex of Lead II.

connection with the well-known rule that II = I + III, the segment *D* of Fig. 15 happens to illustrate the possibility, so often described, of a normal electrocardiogram being built up of two practically monophasic components. This animal died about five hours after the last record was made; there was no evidence of fibrillation, the presumable cause of death being cardiac failure or a gradual fading of the heart automaticity.

Resuming, we may state that after left ligation bundle-branch block was observed, and after right ligation sino-auricular block, auriculoventricular block, and shifting of the pacemaker.

A study of these conduction disturbances tends thus to give rise to the impression that in Macaca the right coronary artery is of greater significance for the higher centers and conduction paths, including the auriculoventricular node, which in man also is supplied principally by

the right artery;[24] while the left artery in this monkey nourishes the lower strands, namely, the bundle branches.

It appears, however, that often the nonligated vessels can function in a compensating way since many ligations were not followed by conduction disturbances, and such disturbances, even if they developed, sometimes disappeared later.

SUMMARY

The arrhythmias and conduction disturbances, observed in several monkeys (*Macaca irus*) after coronary ligation, are described. Extrasystoles were recorded in six out of seventeen monkeys after ligation of the anterior descending branch of the left artery and in six out of fifteen monkeys after ligation of the right artery. The points of origin of the extrasystoles were determined from the electrocardiogram, especially from simultaneous records. The probable cause of these extrasystoles is discussed. Such extrasystoles may, especially if they originate in the apical part of the ventricles and show a tendency to persist for a longer time, bear a localizing character. In two of the monkeys with ligation of the right vessel, ventricular extrasystoles developed into paroxysms of ventricular tachycardia. In one of those a paroxysm could be temporarily checked by a bilateral pressure on the region of the carotid sinus. The possible relation between extrasystoles and fibrillation is discussed. Ventricular fibrillation could be caused experimentally in the monkey by an electrical stimulus at the end of systole. A correlation between extrasystoles and ventricular fibrillation could, however, not be proved with certainty from the observations after coronary ligation. Certainly at least eight of the seventeen monkeys with ligation of the left vessel and two of the fifteen monkeys with ligation of the right vessel died of ventricular fibrillation. The chance of fibrillation after ligation is greatest during the first forty minutes. If it has not developed within about five days, it will probably never set in. Not every death after coronary ligation is due to ventricular fibrillation. Fibrillation after ligation could not be stopped by chemical or physical methods. Bundle-branch block was observed after left ligation; sino-auricular block, auriculoventricular block, and shifting of the pacemaker after right ligation. The relative value of the right and left coronary artery in supplying the different parts of the conduction system in Macaca is discussed.

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THE APPEARANCE OF THE T-WAVE IN LEAD IV IN NORMAL CHILDREN AND IN CHILDREN WITH RHEUMATIC HEART DISEASE

With Some Observations Concerning the Cause of the T-Waves Obtained*

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Chicago, Ill.

THE value of Lead IV in conditions other than coronary disease has received little attention. The preliminary report by Levy and Bruenn,[1] therefore, stimulated us to investigate more systematically the appearance of Lead IV in rheumatic heart disease. We felt that since many of the patients with this disease were children, it might be advisable to determine the appearance of Lead IV in normal children of various ages and to establish criteria for comparison with children having rheumatic heart disease. We found, for example, that an upright T-wave in Lead IV occurred in many normal children, a finding which has been reported independently by Master and his associates[2] and by Rosenblum and Sampson.[3]† This would make the upright T-wave in Lead IV reported by Levy and Bruenn[1] in rheumatic heart disease less significant in children. In the present study an attempt was made also to evaluate the cause for the changed appearance of Lead IV in normal children and those with rheumatic heart disease.

Four-lead electrocardiograms were obtained in 61 normal children and 5 adolescents; in 20 a second record was obtained at a later date to determine the stability of Lead IV. Four-lead electrocardiograms were also obtained in 31 children, 4 adolescents, and 10 young adults suffering from rheumatic heart disease. Records were obtained in 28 of these during the acute stage and in 29 during the inactive stage. In 24 patients serial curves (from two to four) were obtained during the course of the disease.

The technic employed was that previously described by Katz and Kissin[4] and by Bohning and Katz.[5] The electrode was placed in the fourth interspace just to the left of the sternum. In children of five years or younger a smaller sized electrode (1.5 by 5.0 cm.) was used. During the last nine months, we have used the electrode described by Jenks and Graybiel.[6] Controls showed that curves obtained with the three types of electrodes were identical.

The amplitude of the various deflections in Lead IV was measured, using the level of the curve just before the onset of the P-wave as the zero level. In order to evaluate the effect of age on Lead IV, both the normals

*From the Heart Station, Michael Reese Hospital.

†This was first described by P. Moia in Rev. argent. de cardiol. 2: 26, 1935.

and the patients with rheumatic heart disease were divided into five age groups, viz., (1) birth to 5 years, (2) 6 to 10 years, (3) 11 to 15 years, (4) 16 to 20 years (adolescents), and (5) 21 years or over.

RESULTS

1. *Normal children.*—A summary of the findings in Lead IV, in the normal children and adolescents is assembled in Table I. While the number of adolescents is small, the findings in this group fall intermediately between those of the adult and child groups. The range of findings in these normal children is shown in Fig. 1.

The P-wave in Lead IV from our study appears to have the same contour range as in the adult except that upright P-waves were more common. The amplitude of QRS_4 (from its most negative to its most positive point was on the average greater than in the adult. This was due to the fact that the average upright phase of QRS_4 was taller in the normal children than in the adults. The $\frac{Q}{R}$-ratio (the ratio of amplitude

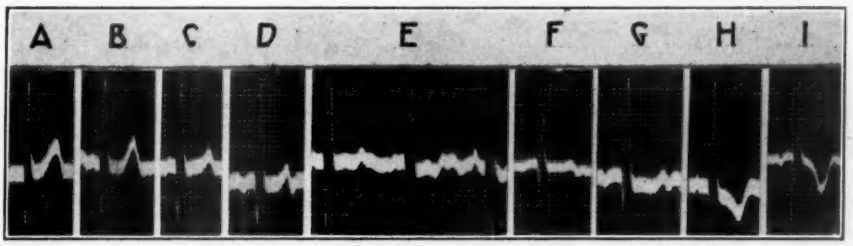


Fig. 1.—Segments of typical Lead IV electrocardiograms obtained from normal children arranged from curves with large upright T-waves on the left to those with inverted ones on the right. The ages of children whose records are shown in segments *A* to *I* are 4½, 1½, 3½, 8, 11½, 13, 10, 15, and 11 years, respectively. Two cycles are shown in segment *E* to show cyclic variation in contour due to respiration. Discussion in text.

of the negative to that of the upright phase of QRS_4) was therefore smaller in children than in the adults. The S-T_4 level range in these children was the same as in adults.

The most striking deviation found, which is in accordance with the finding of Moia, Master, and others and of Rosenblum and Sampson, was in T_4. In contrast with the normal adult groups previously reported by us, in which 49 out of 50 individuals (98 per cent) showed inverted T_4, in the group of normal children only 26 out of 61 (42 per cent) showed inverted T_4. In the others, T_4 was either diphasic (with the first phase upright), polyphasic, or upright. T_4 as high as 5 mm. was not infrequent in the children. An inspection of Table II will show that there is a definite correlation with age: the younger the individual, the more likely he is to have an upright T-wave. The oldest child with an upright T_4 was fourteen years of age.

It follows from this that an upright, diphasic, or polyphasic T_4 in young children, contrary to the findings in adults, cannot by itself be

TABLE I

SUMMARY OF APPEARANCE OF LEAD IV IN NORMAL ADULTS, ADOLESCENTS, AND CHILDREN, AND IN CHILDREN WITH RHEUMATIC HEART DISEASE

		NO. OF INDIVIDUALS	P_4 AMP.* AV.	P_4 AMP.* RANGE	Q_4 AMP. (1ST NEG. DEFLECT. OF QRS_4) AV.	Q_4 AMP. (1ST NEG. DEFLECT. OF QRS_4) RANGE	R_4 AMP. (UPRIGHT DEFLECT. OF QRS_4) AV.	R_4 AMP. (UPRIGHT DEFLECT. OF QRS_4) RANGE	QRS_4 TOTAL AMP. (FROM PEAK OF Q_4 TO R_4) AV.	QRS_4 TOTAL AMP. (FROM PEAK OF Q_4 TO R_4) RANGE	$\frac{Q}{R}$ RATIO (RELATIVE AMP. OF Q_4 TO R_4) AV.	$\frac{Q}{R}$ RATIO (RELATIVE AMP. OF Q_4 TO R_4) RANGE	S-T_4 LEVEL AV.	S-T_4 LEVEL RANGE	T_4 AMP. AV.	T_4 AMP. RANGE
Normal adults†		50	−0.6	+1.0 −1.5	− 8.5	− 1.0 −19.0	+13.5	+ 2.0 +33.0	22.5	5.0 39.0	−	− −	−1.2	0.0 −2.0	−4.4	+ 1.0 −10.0
Normal adolescents		5	0.0	+1.0 −1.5	− 8.0	− 6.0 −10.0	+18.0	+12.0 +21.0	26.0	19.0 31.0	0.5	0.3 0.6	−1.4	−0.5 −1.5	−5.4	− 2.0 − 9.0
Normal children		61	0.0	+2.0 −1.5	− 8.5	− 1.0 −19.0	+17.0	+ 3.0 +40.0	26.0	7.0 57.0	0.5	0.1 2.0	−0.6	0.0 −2.0	−0.3	+ 5.0 − 6.5
Inactive stage	Of rheumatic fever in children	17	0.0	+2.0 −2.0	−11.0	− 4.0 −25.0	+23.0	+ 8.0 +40.0	31.0	15.0 50.0	0.4	0.1 1.7	−0.9	+3.0 −2.0	−1.1	+ 6.0 − 6.5
Acute stage		25	0.0	+2.0 −2.0	− 8.0	− 1.0 −24.0	+21.0	+ 6.0 +40.0	29.0	12.0 50.0	0.4	0.05 2.0	−0.8	+2.0 −3.5	+1.8	+ 6.0 − 4.0

*All amplitude measurements are in millimeters.
No. = number
Amp. = amplitude
Deflect. = deflection
Neg. = negative.
†Taken from the data of Katz and Kissin[4] and Bohning and Katz[5].

TABLE II

APPEARANCE OF T-WAVE IN LEAD IV IN NORMAL INDIVIDUALS AND PATIENTS WITH ACUTE OR INACTIVE RHEUMATIC FEVER CLASSIFIED ACCORDING TO AGE

AGE RANGE	BIRTH TO 5 YR.			6 TO 10 YR.			11 TO 15 YR.			16 TO 20 YR.			21 YR. OR OVER		
Type of case	N	A	I	N	A	I	N	A	I	N	A	I	N	A	I
No. of individuals	14	3	3	17	14	6	30	8	8	5	1	4	50*	2	8
Amp.† of T_4 Av.	+0.9	+2.0	+2.0	+0.6	+1.7	−1.0	−1.1	+1.8	−2.1	−5.4	+2.5	−0.3	−4.4	−1.0	−2.2
Amp.† of T_4 Range	+5.0	+6.0	+6.0	+5.0	+5.0	+6.0	+4.0	+6.0	0.0	−2.0		+3.0	+1.0	0.0	+1.5
Amp.† of T_4 Range	−4.0	−2.0	−5.0	−3.0	−4.0	−6.5	−6.5	−2.0	−5.0	−9.0	+2.5	−2.0	−10.0	−2.0	−6.0
% with upright, di- or polyphasic T_4	71	67	67	58	93	50	50	75	25	0	100	75	2	50	50
% with inverted T_4	29	33	33	42	7	50	50	25	75	100	0	25	98	50	50

*Taken from the data of Katz and Kissin[4] and Bohning and Katz[5]
Amp. = amplitude
Av. = average
% = per cent

N, normal subjects
A, patients with acute stage of rheumatic fever
I, patients with inactive stage of rheumatic fever.
†All amplitude measurements are in millimeters.

taken as evidence of heart disease. Changes in QRS_4 and $S\text{-}T_4$ recognized as indicating abnormality in adults have the same significance in childhood. An upright P_4 in childhood is not uncommon.

2. *Rheumatic Heart Disease in Childhood—Value of Single Records.*—With our analysis of normal children as a base we tried to interpret the findings in children with rheumatic heart disease. The results of the measurements are summarized in Table I. In cases in which more than one curve was obtained in the active stage, the curve used was the one taken when the patient showed the greatest degree of activity. In this analysis abnormalities in rhythm and in A-V and intraventricular conduction were ignored, attention being paid only to the contour and amplitude of the various deflections in Lead IV.

No significant deviation in P_4 was noted in this series as compared with the normal controls. However, large P_4 waves of long duration outside the normal range were found in patients with long-standing mitral stenosis; this was associated with large, broad, upright or diphasic P-waves in the standard three leads. No significant changes in the QRS_4 group were seen in this series except for disturbances in intraventricular conduction, viz., prolongation of QRS_4 span, slurring and notching, and M- and W-shaped complexes. However, QRS_4 complexes mainly up with only small Q_4-waves (first negative phase of QRS_4) were frequently encountered. $S\text{-}T_4$ deviations outside the normal range occurred twice in patients with long-standing rheumatic heart disease; both were elevated above the isoelectric level. In four patients deviations of the $S\text{-}T_4$ segment appeared only in the acute stage; in three of these $S\text{-}T_4$ was elevated; in one it was depressed 3.5 mm. (which is outside the normal limit of 2 mm.).

While the appearance of T in Lead IV was not strikingly different in individual children with rheumatic fever from those in the normal control group, upright, diphasic, and polyphasic T_4-waves were more frequent in rheumatic heart disease, especially in the active stage. This was true in all age groups as shown in Table II. The T-wave in Lead IV showed no peculiarities in rheumatic fever not seen in the normal control children.

From this analysis it would seem that in a single record a tall and broad P_4, an absence of the Q_4 (the first negative phase of QRS_4), deviations of $S\text{-}T_4$ (more than 2 mm. below or any extent above the isoelectric line), prolonged span, marked notching, and triphasic appearance of QRS_4 are the only signs of disease of the heart to be obtained in childhood from Lead IV. None of these abnormalities is specific for rheumatic fever. In contrast to the adult, the contour of the T-wave in Lead IV in a single record is apparently of no diagnostic value in childhood.

3. *Rheumatic Heart Disease—Serial Records.*—Serial curves were obtained in twenty-four patients. While the series is small, certain deduc-

tions seem justified. As the activity of the rheumatic infection subsided, there was a tendency for the first negative phase of QRS_4 to increase in depth; that is, the $\frac{Q}{R}$ ratio increased. This did not occur in

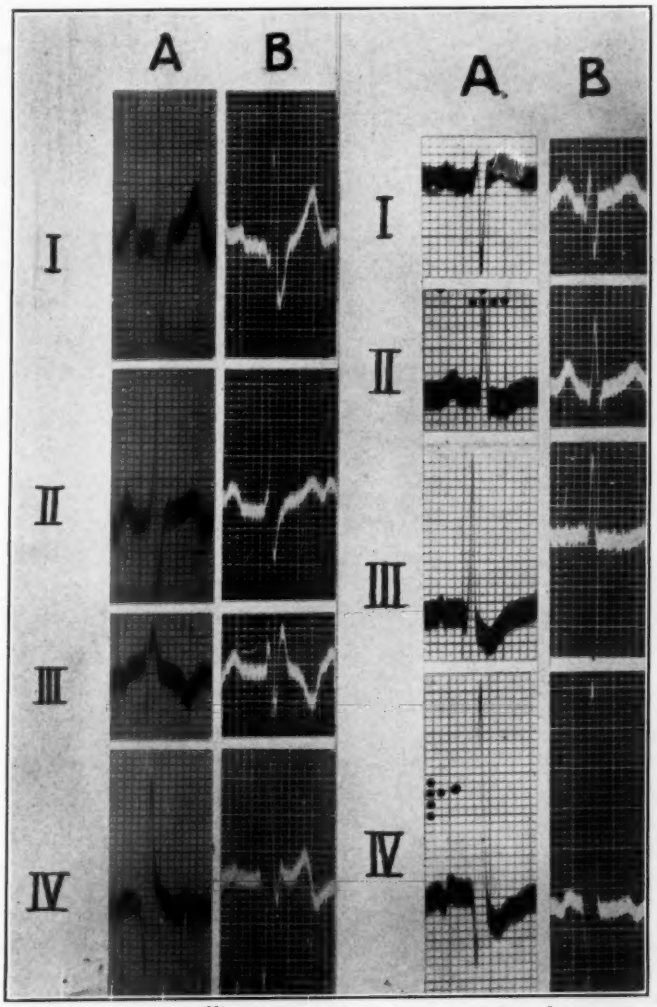


Fig. 2.

Fig. 3.

Fig. 2.—Four-lead electrocardiograms obtained in an eleven-year-old boy with recurrence of acute rheumatic fever and evidence of an old mitral and aortic valvulitis. The acute attack started three weeks before curve *A* was obtained. Curve *B* was obtained a week later. The patient's course was downhill, and he died three weeks after curve *B* was taken. Discussion in text.

Fig. 3.—Four-lead electrocardiograms obtained in a thirteen-year-old girl with active rheumatic fever of several months' duration, who showed congestive heart failure and pericardial effusion at the time curve *A* was taken. Curve *B* was taken two months later, patient being slightly improved. Patient was discharged, improved, one month later. Discussion in text.

every instance but sufficiently frequently to merit investigation in a larger series.

$S\text{-}T_4$ deviations outside the normal range occurred three times in this series. In one patient (Fig. 2) the S-T deviated more from the normal

in later records. This was associated with a progressive intraventricular block; the patient had a persistent septic temperature and died three weeks after the last record was taken. In a second patient the S-T_4 deviation appeared three months after the onset of the active rheumatic fever and the patient died three weeks later. In the third patient (Fig. 3) the S-T_4 deviation appeared during the active stage and disappeared in a later record taken after the patient had improved clinically. The S-T_4 deviation was, in this case, associated with S-T deviations in the standard leads. In the last two patients there was clinical evidence of pericardial effusion, and the changes were probably due to pericardial tamponade (Katz, Feil, and Scott[7]).

As regards the T_4-wave, the patients could be divided into three groups: Group I (thirteen cases) had upright T_4-waves during the acute stage of the rheumatic fever, and the T-waves became diphasic, polyphasic, or inverted as the patients showed clinical signs of improvement (Figs. 4 and 5). In four of these the variation in contour was confined to Lead IV. This is in accord with the observations reported by Levy and Bruenn.[8] In this group the inversion of the T-wave occurred early while the sedimentation rate was still rapid and the clinical signs of activity were definite.

Group II (five cases) showed no change in T_4 in the serial curves. Of these one had an upright T_4; one had an inverted T_4; and three had diphasic T_4-waves. In these patients the standard leads were also normal and did not show any significant changes in the serial records. Three of these patients had evidence of active rheumatic heart disease in the form of valvular involvement. The other two had chorea with very mild rheumatic heart disease.

Group III (six cases) showed inverted or diphasic T_4-waves in the active stage, and later the T-wave became upright. In all of these the standard leads were abnormal in some regard, and the contour in the successive records changed. Four of these patients showed progressive involvement of the heart and persistent activity; two of these died. Two other patients in this group, however, showed signs of decreased activity and clinical improvement (Fig. 6).

Thus, while there is a fair degree of parallelism between the changes in the T_4 and the clinical course, certain discrepancies were present in several instances in Groups II and III.

4. *Normal Children—Serial Records.*—It was because of this discrepancy that we determined to investigate the constancy of Lead IV in normal children. In adults we (Bohning and Katz[5]) found that the contour of Lead IV is constant within narrow limits. In 20 children Lead IV was repeated from six to eight months after the first record; in 10 of these the second record showed no significant deviation from the first (S_1, Fig. 7); in 7 the second record showed a more negative T_4 or a change from an upright to an inverted T_4 (S_2, Fig. 7); in the

other 3 the second record showed a more upright T_4 or a change from an inverted to an upright T_4 (S_3, Fig. 7). In some instances, as in S_2 (Fig. 7), no change in QRS_4 appeared; in others, as in S_3 (Fig. 7), QRS_4 was altered.

Apparently then the T-wave in Lead IV is not as stable in normal children as in normal adults; nor is T as stable in Lead IV as in the

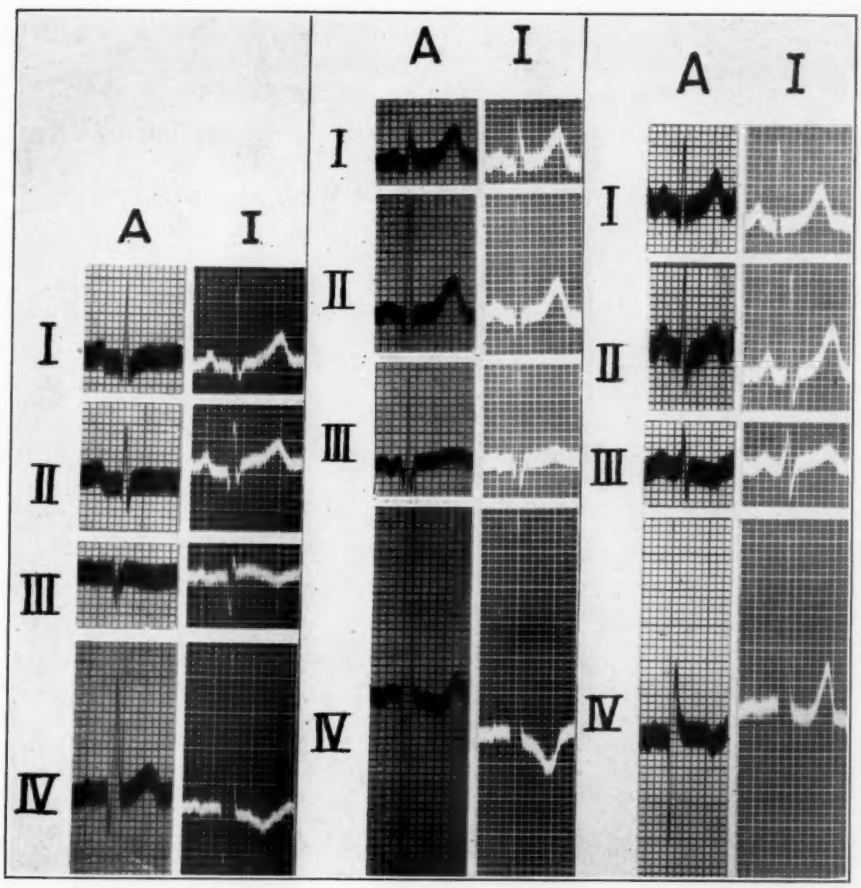


Fig. 4. Fig. 5. Fig. 6.

Fig. 4.—Four-lead electrocardiograms obtained in a nine-year-old boy with a first attack of acute rheumatic fever. Curve *A* taken ten days after onset of symptoms. Curve *I* taken two and one-half months later with patient apparently recovered. Discussion in text.

Fig. 5.—Four-lead electrocardiograms obtained in a four-and-one-half-year-old boy with a first attack of acute rheumatic fever. Curve *A* taken four weeks after onset of symptoms. Curve *I* taken one month later with patient apparently recovered. Discussion in text.

Fig. 6.—Four-lead eletrocardiograms obtained in a two-and-one-half-year-old boy with a first attack of acute rheumatic fever. Curve *A* obtained during acute stage. Curve *I* taken two months later with patient apparently recovered. Discussion in text.

standard three leads of the child. This must be considered in interpreting the effects of acute rheumatic fever and rheumatic heart disease on serial electrocardiograms in children. It helps to explain some of

the discrepancies between the clinical course and the T_4 changes noted above. It would seem, therefore, that even serial electrocardiograms in children with rheumatic heart disease must be cautiously interpreted as evidence of progression or recovery.

DISCUSSION OF FINDINGS, WITH SOME FURTHER OBSERVATIONS AND THEORETICAL CONSIDERATIONS

The explanation for the presence of upright T-waves in Lead IV in normal children must be sought in differences (1) in the position of the heart in the chest due to (a) shift in its anatomical long axis, (b) rotation of the heart on its transverse or sagittal axes, or (c) the relative size and shape of the ventricles; (2) in the contact of the heart with the chest wall, the extent and position of the precordial area not covered by lung, the thinness of the chest wall, or the shape and size of the chest cavity. (Upright T_4-waves tended to be more frequent in children with thin chest walls and narrow thoracic cages.) These various factors can alter the electrocardiogram in Lead IV since the precordial electrode is placed in relation to a bony landmark of the chest and does not bear the same relation to the heart in children that it does in adults.

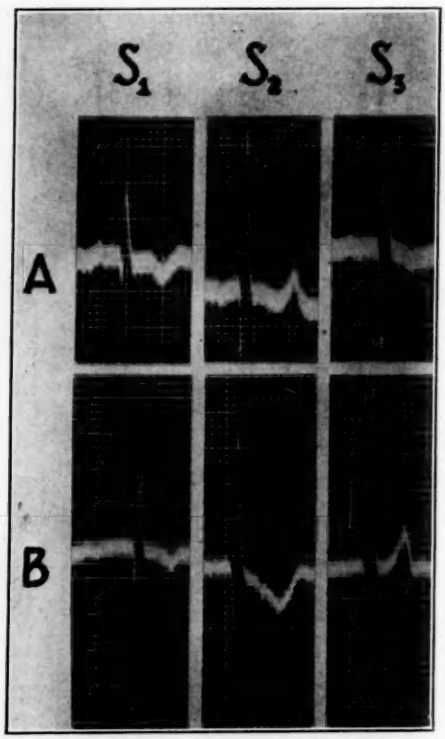


Fig. 7.—Lead IV records obtained in three normal children to show the variability found in some of these normal children when serial curves are taken: S_1, a girl aged eight years; S_2, a boy aged ten years; and S_3, a boy aged five years. Curves *A* were obtained in February, 1935, curves *B*, in October, 1935. Discussion in text.

It is well known that the heart in children differs from the heart in adults in the sense that (a) the ratio of right ventricular weight to left ventricular weight is increased, especially in early childhood, and moderate right axis shift of the electrocardiogram is more common, (b) the heart tends to lie more horizontally, (c) the right ventricle forms more of the left half of precordial dullness and (d) may lie more intimately in contact with the anterior chest wall (Lincoln and Spillman,[9] Bakwin and Bakwin,[10] and Roesler[11]). There is some evidence that these factors might cause the upright T. Thus, White[12] reported that T_4 was usually upright in cor pulmonale and the tetralogy of Fallot. In a series of seven adult patients which we have assembled with right axis shift due to varying types of heart disease such as cor pulmonale, mitral stenosis, congenital heart disease, or displacement of the heart to the right, T_4 was upright only on occasion (Table III). On the other hand, in a series of sixteen adults patients with left axis shift due to hypertension, rheumatic and syphilitic aortic insufficiency, and congenital heart disease, T_4 was inverted in all instances, provided patients with coronary sclerosis were excluded (Table III). In twenty of the normal children a direct correlation was made between T_4 and the axis deviation in the standard leads. Five of these twenty normal children showed right axis deviation, and fifteen did not; 80 per cent of the children with right axis deviation had T_4 upright while only 30 per cent of those without right axis deviation had T_4 upright (Rosenblum and Sampson,[3] however, could obtain no such correlation in fifty children). This correlation together with the observations in adults with right and left ventricular preponderance indicates that axis deviation to the right is an important factor—but not the only one—responsible for the appearance of an upright T_4 in normal children.

Evidence in line with this is the fact that we have found that in the majority of normal adults, upright or diphasic T-waves are obtained when the precordial lead is placed in the fourth interspace to the right instead of the left of the sternum (Table III). This is also the case usually in adults with right axis deviation, but in those with marked left axis deviation the T-wave with this precordial lead is negative (Table III).

These observations and others which we will report in future communications led us to investigate the electrical field during the inscription of the T-wave.

As a start, we took records with the distant electrode on the left leg and the precordial electrode in four different regions of the anterior chest located somewhat like those used by Kossmann and Johnston,[13] all in the fourth intercostal space, to wit: (a) just to the right of the sternum, (b) just to the left of the sternum (the standard Lead IV we employ), (c) in the left midclavicular line, and (d) in the left anterior axillary line. Such records we have now obtained in over 100 patients.

TABLE III

APPEARANCE OF T IN VARIOUS PRECORDIAL LEADS USING THE LEFT LEG FOR THE SECOND ELECTRODE

ADULT OR CHILD	PRECORDIAL LEAD IN 4TH INTERSPACE			
	TO RIGHT OF STERNUM	TO LEFT OF STERNUM	IN MID-CLAVICULAR LINE	IN ANTERIOR AXILLARY LINE
		Normals		
A	+2	−9	−7	−½
A	−2	−8	−7	−2
A	+2	−5½	−6½	−1½
A	−1, +2	−9	−13	−3½
A	+2½	−8	−7	−4
A	+2	−6	−5	0
A	−2, +1½	−5	−3.5	−1
A	−1, + ½	−4½	−3	−1.5
A	−1, +3	−12	−7	−1.5
A	−1, +2½	−5½	−4	−2
C (9 yr.)	+3½	−4	−6	−4
C (10 yr.)	+3	+1, −1	−3	−3½
C (10 yr.)	+5	−2½	−4½	?
C (6 yr.)	+4	−2	−4	−3
C (11 yr.)	+2	−6	−6½	−3
C (7 yr.)	+5	+4	−5	−2
C (9 yr.)	+6	+2	−2	−5
		Right Ventricular Preponderance		
A	+2	−2	−9	+1
A	+½	+½, −½	−1½	−2
A	−1½	−1	+2	−½
A	+6	+5	+7	+1
A	−4	−4	?	+5
A	+2	+3	−7	+3
A	+1	−8	−5	−3
C (5 yr.)	+8	+12	+3, −1	−5
C (15 yr.)	+4½	+3	−2	−1
C (9 yr.)	+6	−6	−7	−5
C (10 yr.)	+8	−6	−12	−5½
C (12 yr.)	+3	+1	−1	−6½
C (13 yr.)	+2	+1½	−1	−1
C (8 yr.)	+3	+2	−3	−4
		Left Ventricular Preponderance		
A	−2	−5	−7	−1
A	−2	−3	−1½	+4½
A	−1½	−4½	−1½	+1½
A	−1	−3	+1	+1
A	−3	−3	+½	+1
A	−2½	−3	−1	+1½
A	−1	−2	+½	+2½
A	−1½	−3	+6	+4½
A	−10	−7	+13	+5
A	−4	−4	−1	+1½
A	−4	−3	+4	+2
A	−6	−13	+4	+10
A	−9	−15	−2	+4½
A	−5	−10	−5	+2
A	−3	−6	−2	+6
A	−3	−10	−3	+4½

For this study we have confined ourselves to an analysis of the height of the T-wave in normal adults and children and those showing right and left ventricular preponderance. The results are assembled in Table III, and the significant findings have already been referred to. It was obvious, after these data were assembled that too few points had been explored to give an adequate idea of the electrical field during the inscription of T. In eleven individuals, therefore, a larger number of points were explored over the chest anteriorly and posteriorly. The subjects were kept in the reclining position while the precordial electrode was shifted, the other electrode being fixed on the left leg. A similar method has been used by Groedel and Koch[14] recently for the QRS complex. Both of these methods are an application of Waller's concept of the electrical field. The electrocardiograms so obtained give the relative potential of the exploring electrode with respect to the leg and not the absolute potential. However, the leg electrode is placed so far from the heart that its potential changes during the inscription of T are not great. An inspection of some of the records reported by Wilson and his associates[15] purporting to give the absolute potential* of the leg shows the magnitude to be within 0.1 millivolt. In determining the potential, the height and direction of the T-wave were used. It is appreciated that the time of inscription of this point is not synchronous in the different precordial leads employed. But this error is also of little significance for the use we intend in this report. While our method, for the reasons given, is to be considered only a first approximation, it nevertheless revealed definite information. More precise exploration of the electrical field for all phases of the heart cycle is in progress in this laboratory and will be reported at another time.

The data obtained in several subjects are shown diagrammatically in Figs. 8 to 14. In Fig. 8 is shown the potential of various regions in a twenty-three-year-old adult with normal standard leads and with a Lead IV well within the mean of normal limits. The line defining the potential equal to that in the leg is clearly shown. It is interesting that the line of "leg potential" runs cephalad in the midsternal line to the level of the third rib and then runs obliquely upward over toward the left arm, reaching its crest at the level of the second rib and then running obliquely downward toward the back. In the back it descends somewhere along a line over the left scapular angle. In this subject the relatively negative potential (the height of the upright T-waves) was nowhere as great as the relatively positive potential (the depth of the negative T-waves), but the area in the chest occupied by the former was much greater. Furthermore, the lines of equipotential (equal T-wave amplitudes) are much closer over the sternum and precordium than elsewhere.

In Fig. 9 is shown a similar analysis of a child aged nine and one-half years who had a negative T_4; the electrical field during the peak

*This idea of Wilson's has recently been seriously questioned by Storti.[16]

Fig. 8.

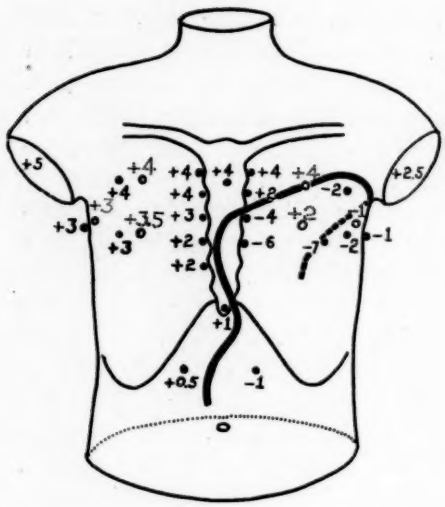
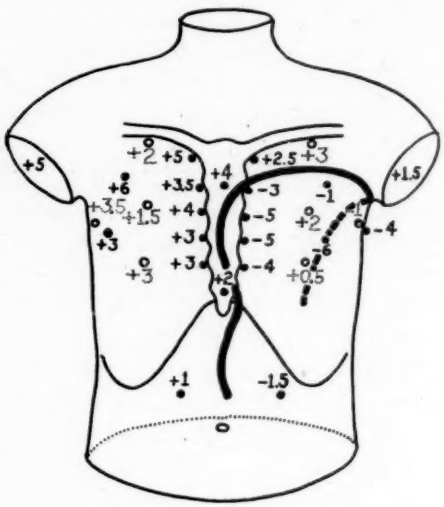


Fig. 9.



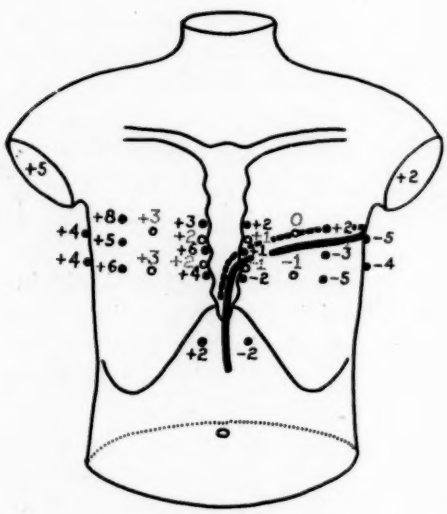


Fig. 10.

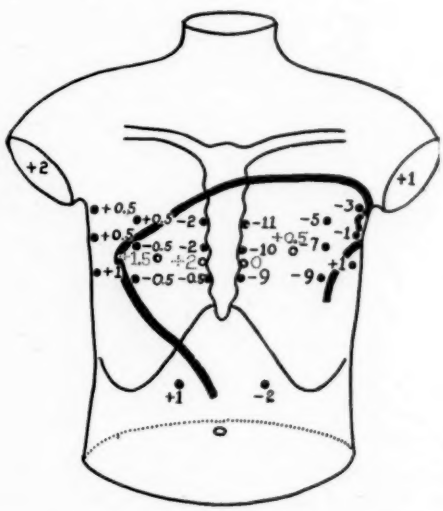


Fig. 11.

Fig. 8.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of leg in a normal twenty-three-year-old man with a normal four-lead electrocardiogram. (+ indicates an upright and −, an inverted T-wave). Solid circles and solid figures are on anterior surface or anterior half of lateral surface of chest, open circles and dotted figures, on posterior surface or on posterior half of lateral surface of chest. Heavy line marks the course of potential during peak of T equivalent to that in leg, the so-called "leg potential" line. It is marked out as a solid line when on anterior surface or anterior half of lateral surface and is marked out as a dotted line when on posterior surface or posterior half of lateral surface of chest. Discussion in text.

Fig. 9.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a normal nine-and-one-half-year-old child with T_4 inverted. Conventions as in Fig. 8. Discussion in text.

Fig. 10.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a normal nine-year-old child with T_4 upright. Conventions as in Fig. 8. Discussion in text.

Fig. 11.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a fifty-six-year-old man with marked left ventricular preponderance. Conventions as in Fig. 8. Discussion in text.

Fig. 12.

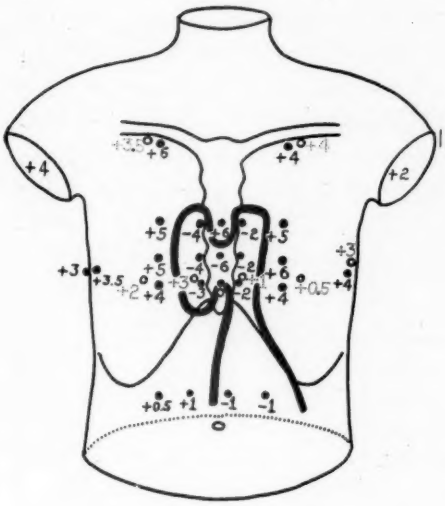
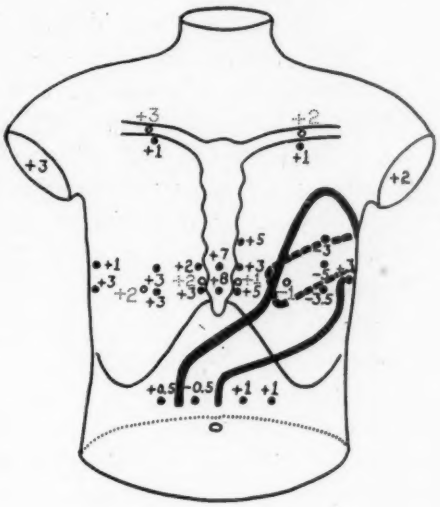


Fig. 13.



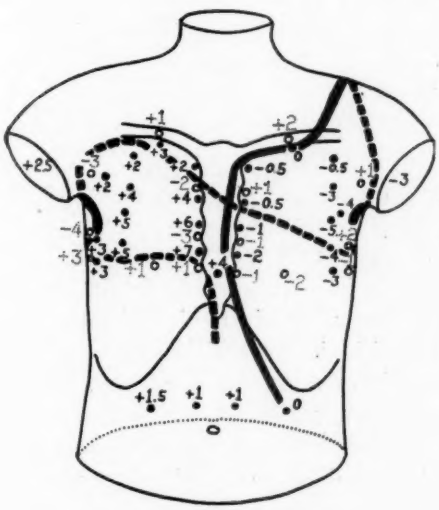


Fig. 14.

Fig. 12.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a forty-eight-year-old man with right ventricular preponderance. Conventions as in Fig. 8. Discussion in text.

Fig. 13.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a forty-six-year-old woman with right ventricular preponderance. Conventions as in Fig. 8. Discussion in text.

Fig. 14.—Diagram showing the magnitude of the T-wave in various spots on the chest (and in the two arms) as compared with that of a leg in a fifty-year-old man with congenital heart disease, having QRS inverted in all three of the standard leads. Conventions as in Fig. 8. Discussion in text.

of T and the line of "leg potential" was practically, though not absolutely, the same as in the preceding adult. In Fig. 10 is shown a similar analysis of one child aged nine years who had a positive T_4. It will be seen that more of the chest points have upright T-waves than are shown in the preceding two charts and that the line of "leg potential" does not rise as high on the chest as in the preceding subjects. In a second child aged seven years who had a positive T_4, the line of "leg potential" had shifted to the left anterior axillary line and went as high as the second interspace. Unfortunately the posterior part of the chest in this child had not been explored, but the T-wave was upright over the entire chest anteriorly.

In both patients with left ventricular preponderance, the T-wave was negative over the anterior chest wall and positive over the lateral and posterior walls. The line of "leg potential" was near both lateral walls of the chest and crossed high up on the chest anteriorly (Fig. 11). In right ventricular preponderance, of which we have analyzed two cases with, and two without congenital heart defects, the area over which negative T-waves are obtained was markedly reduced (Figs. 12 and 13), but in each the line of "leg potential" took a different course.

The changes described in these conditions might all be conceived as simply being due to a complex rotation of the resultant vector set up in the heart. That this simple concept cannot suffice is shown by the fact that exploration of the field in a fifty-year-old subject with congenital heart disease having inverted QRS complexes in the standard three leads showed a very complex arrangement of the line of "leg potential" (Fig. 14). In viewing the chest at most horizontal levels, four lines of "leg potential" are seen separating areas having positive, from those having negative, T-waves. This observation, however, would fit with the concept promulgated in this laboratory (Katz and Korey[17]) that the electrical field is determined in large part by the nature of the electrical conductors in contact with the heart. According to the study upon which this concept was based, the lungs are poor electrical conductors while the posterior paravertebral muscle mass, the diaphragm, and the anterior chest wall where lung is absent are the good conductors. Thus in this patient with congenital heart disease it would seem that the currents set up from the posterior good conductors and those set up from the diaphragm and anterior chest wall interfere with each other so that the result might be regarded as similar to the action of two bipoles not in line. Investigations are in progress to see whether this holds also in other conditions. At present we can say that there is no evidence opposed to the idea that the electrical field in all cases is the resultant of currents spreading in the body from various regions of the heart in contact with good conductors. When the position of the heart is altered in relation to these good and poor electrical conductors

and when the position in these good and poor electrical conductors in the chest is altered, the whole electrical field is changed. The effect would be more marked over the chest since the lines of equipotential are closer together than in the extremities.

The division of children into those having a negative T-wave and those with a positive T-wave in Lead IV fits the clinical and x-ray observations that children can be divided into those with "puerile" and those with "adult" chests, and that the adult type of chest occurs as early as four years.[18] It is thus possible in children to have the line of "leg potential" run anteriorly anywhere from the middle of the sternum to the left anterior axillary line and have the crest at any level. The variations of T_4 in different normal children can be explained on the variable degree of transition from the "puerile" to the "adult" chest type.

The variability of T_4 contour in successive records of the same child is also to be accounted for on the basis that the line of "leg potential" is close to the position of the precordial electrode ordinarily used in Lead IV and that the lines of equipotential are close together in this locality. Consequently the electrical field could be altered sufficiently by changes in the position of the heart such as might result from shifts in the diaphragm because of gas or food in the gastrointestinal tract, or might result from small differences in posture of the body when the several records were taken. Since the heart in the child is more mobile than in the adult, such changes in T_4 are more to be expected in children than in adults. Respiratory changes of T_4 in children are very common and are more marked than in adults.

The contour of T_4 in acute rheumatic heart disease is determined not only by the factors enumerated above for the normal children but also by two other factors. The first is the result of the active infection of the myocardium. In rare instances it may be the result of pericarditis with effusion or still more rarely of coronary endarteritis with resultant local areas of myocardial ischemia. The second is the result of long-standing involvement of the heart, either the result of the myocardial damage or of changes in heart size, shape, and position which cardiac dilatation and the associated mitral and aortic valvular deformities may have led to. The changes due to the active process tend to disappear when the activity of the infection subsides and are progressive if the acute process advances. The changes due to the chronic damage persist after the active stage has disappeared and change but slowly.

The only clinical problem in rheumatic heart disease as far as Lead IV is concerned is to differentiate changes due to the rheumatic process from those which are normal in childhood and to determine whether changes in successive records are evidence of changes in the rheumatic process and its effects or are normal variations to be encountered in children.

SUMMARY AND CONCLUSIONS

1. Upright diphasic or polyphasic T-waves in Lead IV are common in normal children, especially in the younger age groups.

2. The contour of Lead IV in normal children may alter considerably when curves are repeated a few months apart.

3. Children with active rheumatic heart disease show a higher percentage of upright T-waves in Lead IV than do normal children of the same age. The T-wave tends to become inverted when recovery from the acute stage sets in and tends to become more upright when the disease process becomes aggravated. However, exceptions to these correlations are not uncommon.

4. An analysis was made of the factors which may be responsible for the differences in the T-wave of Lead IV between children and adults, as well as between normal children and children with rheumatic heart disease.

5. The electrical field at the surface of the body during the inscription of the T-wave was examined in a variety of conditions, with the result that a new view concerning the causes and significance of the upright and inverted T-waves in precordial leads was revealed.

6. As a result of the present study, it is concluded that the practical value of Lead IV in children suffering from rheumatic heart disease is definitely limited. Single records in individual cases add no valuable information, and serial curves supply data which may be suggestive and are only confirmatory to that obtained from the ordinary standard three leads.

We are indebted to the medical staff of the Sarah Morris Hospital for Children and of the Children's Cardiac and Pediatric Clinics in Mandel Clinic for their courtesy in permitting us to study their patients. The assistance of Dr. H. Wachtel is acknowledged.

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Department of Clinical Reports

THROMBO-ANGIITIS OBLITERANS IN WOMEN

Report of a Case*

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THROMBO-ANGIITIS obliterans rarely affects women. The reason for this is obscure. In view of what is known about the relationship of smoking to thrombo-angiitis obliterans, it is easy to assume that the smaller incidence of this vascular disease among women is due to the fact that fewer women are smokers. Acceptance of this explanation would need to be based on data indicating that the ratio of the number of men smokers to women smokers approaches the ratio of the number of men with thrombo-angiitis obliterans to the number of women with this disease.

We have studied the records of 200 women between the ages of thirty and fifty years who were examined consecutively at the Mayo Clinic in 1935. Twenty-four of these women (12 per cent) smoked tobacco. In a comparable study of the records of 200 men, 140 (70 per cent) were smokers. This agrees closely with the results of Barker's study in 1931,[1] who found that 69.2 per cent of men were smokers. Barker's study likewise showed that, of 350 male patients with thrombo-angiitis obliterans, four, or 1.1 per cent, were nonsmokers. The ratio of men smokers to women smokers in our series of patients without thrombo-angiitis obliterans is approximately 6:1 (140 men to 24 women). This ratio is much smaller than that of men with thrombo-angiitis obliterans to women with thrombo-angiitis obliterans, which, according to various authors, is from 70:1 to 500:1. It appears, therefore, that tobacco smoking does not explain the differential sex incidence of thrombo-angiitis obliterans. The time element in smoking, however, may be important. It is probable that the women in our series had not smoked tobacco as long as had the men. If the smoking of tobacco is the sole etiological factor in thrombo-angiitis obliterans, it is safe to predict that within the next few decades many more women with thrombo-angiitis obliterans will be observed and that the ratio of women with this disease to men with the disease should approach the ratio of women smokers without thrombo-angiitis obliterans to men smokers without the disease, which is about 1:6 at the present.

Worthy of note in attempting to explain the difference in incidence of thrombo-angiitis obliterans in the sexes is the experimental work of

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McGrath.[2] Female rats were poisoned with ergotamine until gangrene of the tail occurred. If theelin were injected into these animals, the same amounts of ergotamine did not cause gangrene. Theelin did not, however, protect male rats from ergotamine-induced gangrene.

In 1932 Horton and Brown[3] collected from the literature seven cases of thrombo-angiitis obliterans affecting women, and they presented at that time ten additional cases from a series of 700 cases of thrombo-angiitis obliterans observed at the clinic. We agree with Horton and Brown that only Cases 1, 2, and 3, of those which they collected from the literature, are acceptable. Two of these three cases were reported by Buerger[4] in 1924, the other was reported by Meleney and Miller[5] in 1925. Cases reviewed by Horton and Brown which were reported earlier by Koyano,[6] by Telford and Stopford,[7] by Trabaud and Chaty,[8] and by Trabaud and Mredden[9] do not, in our opinion as well as that of Horton and Brown, fulfill the minimal requirements for the diagnosis of thrombo-angiitis obliterans. The data given by Dürck[10] in 1930, in his report of a case of thrombo-angiitis obliterans affecting a woman, are entirely inadequate for such a diagnosis. The case seems to have been only one of superficial phlebitis, affecting a Jewess twenty-seven years old, who used tobacco excessively. Of the ten cases reported from the clinic by Horton and Brown in 1932, in some, all of the characteristics of the disease, as it is encountered in men, were present. In 1935, Silbert[11] reported two cases of thrombo-angiitis obliterans affecting women. His first case, however, is an example of unilateral occlusive arterial disease suggesting arterial embolism.

The total number of cases reported as thrombo-angiitis obliterans affecting women is twenty. In several instances the authors themselves reported uncertainty regarding the diagnosis. We are adding the following case which impresses us as being unquestionably an example of thrombo-angiitis obliterans affecting a woman. This is the first case observed at the clinic since the report of Horton and Brown. In addition, two questionable cases have been observed here. During the intervening time approximately 350 cases of thrombo-angiitis obliterans have been observed.

REPORT OF CASE

A Scandinavian woman, forty-one years old, was admitted to the clinic in September, 1935. There was no family history of vascular disease. She had had typhoid fever at the age of four years, frequent attacks of tonsillitis until she was twenty-five, and at the age of nine years rheumatic fever, which had confined her to bed for four months. She had smoked from ten to fifteen cigarets daily for ten years prior to her admission. In the two years before admission she had noted coldness of the distal half of the left leg and of the left foot and toes. As a result of exposure to cold, the distal half of the left foot and the toes had in turn become pale, cyanotic, and red. Associated with these vasomotor disturbances

numbness and aching pain had occurred. Even getting from bed onto a cold floor induced changes in color; as a result, the patient had learned to put on her shoes before getting out of bed. In the six months prior to admission walking from four to six blocks had produced aching pain in the distal half of the left foot and calf of the left leg; this necessitated rest, which had produced relief in a few minutes. Because of such pain the patient had almost entirely discontinued walking. For a year the first toe of the right foot had been numb and at times quite cold; also, the vasomotor changes just described had involved the third finger of the left hand, which ached after exposure to ice or cold and was numb at times even without exposure. The skin of the dorsal portion of the left foot and toes had cracked and peeled a few weeks before admission.

On physical examination the patient looked well; she was 63 inches (160 cm.) tall and weighed 142 pounds (64.4 kg.). The blood pressure in millimeters of mercury was 136 systolic and 80 diastolic. General examination gave negative results except for indicating the presence of a left Horner's syndrome, which had been present since childbirth nineteen years before.

Examination of the arteries for pulsations* revealed the following: right and left femoral and right and left popliteal, grade 4; right dorsalis pedis, 1; left dorsalis pedis, 0; right posterior tibial, 2; left posterior tibial, 0; right ulnar, 4; left ulnar, 0; right radial, 4; and left radial, 4 (Table I). The compression test devised by Allen[12] was positive for the left ulnar artery. Elevation of the left foot produced pallor, grade 3, and lowering caused rubor, grade 3; the color returned slowly. There was marked decrease in the angle of circulatory efficiency. An area of superficial phlebitis was present on the dorsum of the left foot.

Roentgenograms of the left foot and leg revealed a few small phleboliths at the level of the middle third of the tibia. Routine laboratory studies, including a serological test for syphilis, determination of hemoglobin, enumeration of the erythrocytes and leucocytes, and urinalysis, gave negative results. A diagnosis of thrombo-angiitis obliterans was made.

TABLE I

PULSATIONS IN PERIPHERAL ARTERIES*

ARTERY	RIGHT	LEFT
Femoral	4	4
Popliteal	4	4
Dorsalis pedis	1	0
Posterior tibial	2	0
Ulnar	4	0
Radial	4	4

*4 represents normal pulsation; 0, complete absence of pulsations.

COMMENT

The age of onset of symptoms, the presence of rather characteristic vasomotor disturbances and typical intermittent claudication, the occlusion of the large arteries, the presence of superficial phlebitis, the absence of demonstrable sclerosis, and the apparently progressive nature of this condition, leave no doubt concerning the clinical diagnosis of thrombo-angiitis obliterans. The use of smoking tobacco is supportive evidence for the diagnosis.

*Graded from 0 to 4; 4 denotes normal pulsations and 0 denotes complete absence of pulsations.

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FATAL DIGITALIS POISONING OCCURRING IN A NORMAL INDIVIDUAL*

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THE purpose of this report is to describe a case of fatal digitalis poisoning in a normal individual. The electrocardiogram of this patient presents alterations which will be described in detail. It is hoped that comparison of these changes with the electrocardiographic alterations resulting from therapeutic doses may be of value in preventing overdosage of digitalis.

William Withering[1] in 1785 reported that very large doses of digitalis caused slow pulse, green or yellow vision, convulsions, syncope, and death.

Cohn[2] in 1915 described electrocardiographic changes associated with digitalis therapy which developed in the T-wave in individuals with "an early rather than advanced stage of heart disease." These changes consisted of lowered amplitude of the T-waves, first in Lead III, later in Lead II. In some instances the T-waves became diphasic.

White[3] administered from 2.0 to 3.0 gm. of digitalis leaves to five normal young adults. The amplitude of T, especially in Lead II, was decreased, and later the P-R interval was increased.

Berger[4] reported a patient with mild rheumatic heart disease who received approximately 64 gm. of digitalis in a month. The patient developed nausea, vomiting, yellow vision, electrocardiographic signs of "too much digitalis" (i.e., partial A-V block, depressed S-T segments in Leads I and II), and died suddenly.

Human fatalities resulting from strophanthin are summarized by Robinson.[5] Sollmann[6] reported that 2.5 gm. taken at one dose proved fatal. Levine and Cunningham[7] studied digitalis toxicity in cats and concluded that the margin of safety (the difference between the percentage causing death and that responsible for the earliest evidence of toxicity) averaged 48 per cent. It must be remembered that these investigators were studying animals with normal hearts. Lewis[8] stated that he has seen more than one instance of avoidable death which resulted from failure to withdraw digitalis when "excessive slowing or coupling occurred." White[9] warns that a considerable percentage of the lethal dose has been given when the electrocardiogram reveals excessive inversion of the T-wave and S-T segment, prolongation of the P-R interval, intraventricular block, bigeminal rhythm, or ventricular tachycardia.

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Cushny[10] has described fully the toxic manifestations of excessive digitalis administration in animals. There was an initial rise of arterial blood pressure followed by a pronounced fall, and a variety of arrythmias developed. Other toxic manifestations were marked depression of the respiratory center, muscular weakness, and visual disturbances, probably of central nervous system origin, and finally ventricular fibrillation was followed by marked ventricular dilatation and cardiac standstill.

CASE REPORT

The present report concerns a woman, thirty-one years old (Case No. 48529), who was admitted to the hospital three hours after taking the entire contents (about 300 grains) of a 6-8 oz. bottle of tincture of digitalis for suicidal purposes while acutely intoxicated.

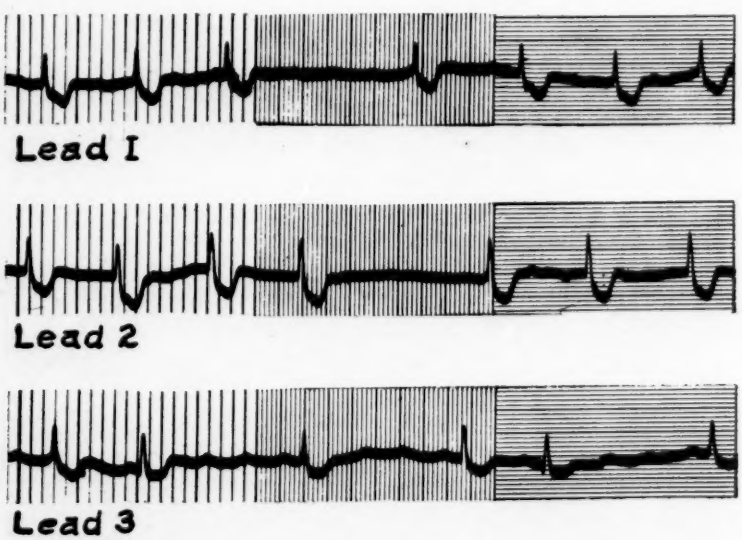

Fig. 1.—Complete A-V dissociation; auricular rate 170; ventricular rate 60 to 70; marked depression of S-T segments in Leads I and II. Inversion of T-waves.

The patient's earlier history was entirely normal. The digitalis had been recently purchased by her father who presumably had heart disease. Three hours after taking the digitalis she became nauseated, vomited a greenish material, and was brought to the hospital. Gastric lavage with tannic acid was carried out, and apomorphine, gr. $\frac{1}{10}$, was administered.

On admission she was semistuporous. Temperature 101.4° F. (rectal), respirations 24, pulse 124, blood pressure 120/75. The pupils were equal, regular and reacted to light and accommodation; the tongue was covered with green coating. The neck showed no venous distention. The admitting physician stated that the cardiac rhythm was absolutely regular but that there was marked variation of the intensity of the heart sounds, runs of loud beats were followed by runs of distant, muffled beats. The reflexes were diminished (alcohol?).

Nine hours later when examined by one of us the pulse was grossly irregular, and there was coincident absence of heart sounds in the absence of the radial pulse. The

heart was of normal size on percussion. No murmurs were heard. The blood pressure was 120/50. The clinical diagnosis of partial heart-block was confirmed by an electrocardiagram.

The patient continued to be nauseated and vomited frequently, remained semi-stuporous, and did not respond to stimulants (caffeine, atropine and adrenalin). The pulse disappeared in twelve hours and continued to be imperceptible. The heart sounds were distant and of varying intensity. The respirations were slow and irregular. During the twelfth hour the patient had two mild convulsive seizures; respirations ceased; cyanosis increased but heart action continued irregularly. Artificial respiration was given for five minutes; during this time the heart sounds could be heard; and the heart rate was accelerated by intracardiac adrenalin. Death occurred from respiratory failure.

Unfortunately, permission for autopsy could not be obtained.

The electrocardiogram is reproduced in Fig. 1, and shows an auricular rate of 170 with complete auriculoventricular dissociation, the ventricular rate averaging 66 per minute. The S-T segment take-off is conspicuously low in Leads I and II and is depressed in Lead III. Thus, there is no reciprocal relationship between Leads I and III as is frequently encountered in coronary occlusion. The negative T-waves are merged with the S-T segment. As the maximum effect on the T-waves usually occurs about six hours after any one dose of digitalis (Pardee[11]), the changes in this record are probably maximum. However, the significant and unusual change is the very low take-off of the S-T segments.

DISCUSSION

As far as we can ascertain, this is the first recorded electrocardiogram in fatal digitalis intoxication in a normal individual. The auricular rate of 170, with an idioventricular rate of 60 or 70 in the presence of complete heart-block, is unusual. This is of especial interest as it is generally thought that large doses of digitalis produce bradycardia.

The nausea, the vomiting, and the respiratory character of death appeared to be related to the "central" action of digitalis on the nervous system rather than to peripheral action on the heart itself. Of especial interest was the period of apparent clinical improvement four hours before death and the *modus exitus* with respiratory failure.

SUMMARY

Death from respiratory failure occurred in a normal individual twelve hours after the ingestion of approximately 300 grains of digitalis. Auricular tachycardia, A-V block, and marked depression of S-T segments were shown electrocardiographically.

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Department of Reviews and Abstracts

Selected Abstracts

Schade, H.: The Transmission of Pulsations from Arteries to Veins and Its Bearing on the Circulation of Blood. Ztschr. f. Kreislaufforsch. **28**: 144, 1936.

This report, compiled posthumous by O. Hepp, is based on extensive studies of animals and models. Work on models demonstrated that the efficacy of the transfer of the pulsation from arteries to veins increases as the arterial pulse amplitude and the pulse frequency are increased until optimum values are reached.

Animal experiments and roentgenological studies in man demonstrated pulsatory fluctuations in blood velocity in the peripheral veins. These were synchronous with the arterial pulse. In the presence of functionally efficient venous valves, these pulsations in the veins cause an effective acceleration of flow toward the heart. Changes in tone of the veins and in the degree of extravascular support offer an automatic regulation of the transmission of the pulsations from the arteries to the veins. Records of peripheral venous pulsations were obtained with a special sphygmograph which excluded the possibility of retrograde transmission from the heart. These peripheral venous pulses were of relatively small amplitude.

L. N. K.

Palme, F.: Action of Adrenalin on the Carotid Sinus. Ztschr. f. Kreislaufforsch. **28**: 173, 1936.

Topical application of 1:1,000 adrenalin solution to the exposed carotid sinus of the rabbit caused a protracted hypertension.

L. N. K.

Walter, J.: Effect of Calcium on Adrenalin Reaction. Arch. di. sc. biol. **38**: 300, 1935.

Experiments were conducted on perfusion of the isolated rabbit's ear and frog's limb. The normal calcium chloride content of the perfusing fluid was 0.2 per cent for the rabbit and 0.1 per cent for the frog. A fourfold increase in the calcium caused vasoconstriction; absence of calcium caused vasodilation; and subsequent restoration of calcium, marked vasoconstriction. A decrease in the calcium reduced the normal vasoconstrictor response to adrenalin (1 to 10 million for the rabbit, 1 to 5 million for the frog). Increased calcium content had a different effect in the two cases.

E. A.

Smith, Dietrich C., and Mulder, Arthur G.: The Effect of Accelerator Nerve Stimulation and of Adrenalin on Recovery From Ventricular Fibrillation in the Cat. Am. J. Physiol. **115**: 507, 1936.

In cats spontaneous recovery from ventricular fibrillation following faradization of the ventricles occurs in the large majority of animals.

Evidence is presented to show that the time of fibrillation varies directly with the weight of the cat (size of the heart).

Stimulation of the accelerator nerves during ventricular fibrillation in the cat shortens the duration of the fibrillation.

While the heart is under the influence of adrenalin, recovery from fibrillation following faradization of the ventricles is instantaneous.

AUTHOR.

Nicolai, L., and Hantschmann, L.: On the Stereostethoscope. Klin. Wchnschr. **15:** 91, 1936.

The stereostethoscope differs from the common model in that it has two stethoscope receivers, one leading to each ear. In ausculting murmurs which are difficult to locate, the relative intensity of the murmur heard in each ear gives an idea of the place of origin of the sound. Clinical trial with heart murmurs and pulmonary râles have proved useful in helping to locate the origin of these sounds.

R. K.

Duomarco, J.: Relationship of Mean Arterial and Intraventricular Pressure to Cardiac Output. Compt. rend. Soc. de biol. **121:** 553, 1936.

The ratio of the intraventricular mean pressure to the mean arterial pressure is a criterion of cardiac efficiency. When this value is greater than 0.5, it may be due to limitation of ventricular distention by pericardium, by excesses of work, or by injury.

E. A.

Sigler, Louis H.: Further Observations on the Carotid Sinus Reflex. Ann. Int. Med. **9:** 1380, 1936.

Slowing of the heart induced by the carotid sinus reflex was studied in 426 cases, which were divided into seven groups: (1) arteriosclerotic heart disease; (2) hypertension and hypertensive heart disease; (3) arteriosclerotic and hypertensive heart disease; (4) rheumatic heart disease; (5) psychoneurotic heart disease; (6) other forms of heart disease or disturbances; and (7) general constitutional disturbances. Various conditions arranged in order of greatest frequency and degree of slowing induced by the carotid sinus reflex follow: arteriosclerotic and hypertensive heart disease, rheumatic heart disease, general constitutional disease, psychoneurotic and miscellaneous heart disease. Hypertension seems to increase the frequency but diminish the degree of the carotid sinus reflex. The cardio-inhibitory reflex appears to depend on a constitutional vagotonic tendency, which is more marked among males and develops with advancing age. General toxic or irritative states, endocrine factors, intracarotid blood pressure, and local disease, or disturbances in the heart itself seem to play a part in sensitizing the reflex.

AUTHOR.

Wright, Irving S., and Lilienfeld, Alfred: The Pharmacological and Therapeutic Properties of Crystalline Vitamin C (Cevitamic Acid) With Especial Reference to Its Effects on the Capillary Fragility. Arch. Int. Med. **37:** 241, 1936.

After a preliminary review of the nature and properties of crystalline vitamin C (cevitamic acid), with a brief discussion of some of the therapeutic claims made for the substance, the authors give their experience with cevitamic acid, particularly in the treatment of certain of the hemorrhagic diseases. As an aid to the diagnosis of vitamin C malnutrition, the authors describe a capillary fragility test which is a modification of the tourniquet test performed under standard conditions. With

this technic a normal result shows not more than ten petechiae within a delimited area of skin. Ten to twenty is a marginal zone, and a count above twenty appears to be definitely abnormal.

The authors feel that a history of scanty vitamin C intake, together with an increased capillary fragility, which decreases definitely on the administration of vitamin C, is fair presumptive evidence of vitamin C malnutrition. Cevitamic acid was found to be of great value in clinical and "subclinical" scurvy, and apparently of no value in thrombocytopenic purpura and hemophilia.

AUTHOR.

Kayser, G., and Weber, A.: Registration of Heart Sounds and Their Reproduction by Means of the Phototone Technic. Munchen. med. Wchnschr. **82**: 1032, 1935.

Heart sounds are recorded on moving film by means of a microphone. They can be reproduced by running the film past a photoelectric cell which is connected through an amplifier with a loud-speaker or ear phone. This method is valuable for teaching purposes and permits the combination of auditory and visual examination of the heart sounds. When the sounds are recorded simultaneously with the electrocardiogram, it permits better timing of murmurs, a clearer interpretation of the type of third heart sound or gallop rhythm present. A visual record picks up low pitched sounds which the ear may not hear.

L. N. K.

Pereira, J. C.: Phonocardiographic Studies in 50 Normal Pregnancies. Rev. argent de cardiol. **2**: 323, 1935.

The heart sounds (Wiggers and Dean), the venous pulse (Frank) and the electrocardiogram (D 1) were simultaneously recorded in fifty normal pregnant women. The heart rate, duration of systole, and systolic-diastolic relation were found to show no significant differences as compared with those found in young male adults. In 62 ± 4.6 per cent of the cases only the first and second sounds were recorded; in 22 ± 3.98 per cent the first, second, and third sounds were recorded; in 10 ± 2.85 per cent the auricular, first, second, and third sounds were present in the records and in 6 ± 2.2 per cent the auricular, first, and second sounds were recorded.

Comparing these data with those gathered by Braun Menendez and Orias in healthy male young adults, it becomes apparent that the third normal sound is less frequently recorded in normal pregnant women while the auricular sound is recorded with about the same frequency. No reduplication of either the first or second sound was recorded. In two cases in which direct auscultation indicated a reduplication of the second sound, a third physiological sound was recorded.

AUTHOR.

Snellen, H. A.: Conduction Disturbances in the Auricles. Ztschr. f. Kreislaufforsch. **28**: 234, 1936.

A case is described of a forty-two-year-old woman with marked congestive failure, in whose electrocardiogram extra waves were present interspersed among the regular PQRST waves. These extra waves occurred at a regular slow, constant rate (about 45 per minute). The author interprets these waves as originating in an auricular pacemaker which controls a region of the auricles blocked off from the rest of the auricles and from the ventricles. At autopsy the right ventricle was found dilated and hypertrophied. However, the coronary arteries, the auricles, and the myocardium were found to be normal.

L. N. K.

Tigges, Franz: The Electrocardiogram in Anoxemia. Ztschr. f. Kreislaufforsch. **28**: 225, 1936.

This report deals with a study of (1) the effect of placing fifteen normal persons in low pressure chambers and reducing the pressure in the chamber to an equivalent of 5,000 to 7,000 meters above sea level, (2) the effect of reducing the content of O_2 in inspired air to as low as 8 per cent in thirteen experiments on normal persons, and (3) the effect of inhalation of pure oxygen in six experiments with cyanotic patients.

Anoxemia, sufficient to produce mountain sickness, caused acceleration of heart rate, shortening of the P-R and QRST intervals, augmentation in the size of the P-wave, and flattening of the T-wave. On relieving the anoxemia, the deviations were restored to and temporarily beyond the normal values. No particular electrocardiographic changes marked the onset of mountain sickness. Oxygen inhalation in cyanotic patients caused changes the reverse of those seen in normal individuals rendered anoxemic.

L. N. K.

Hinrichs, Alfred: The Differential Diagnosis of A-V Nodal Rhythm. Ztschr. f. Kreislaufforsch. **28**: 205, 1936.

This is a case report of a thyrotoxic patient having a tonsillar abscess, who developed an incomplete A-V block with Wenckebach periods. The next day he had a regular rhythm with a rate about 110 beats per minute. The P-wave followed the QRS complex by about 0.20 sec. simulating (A-V) nodal rhythm. Analysis showed, however, that this was in reality a sinus tachycardia with a markedly prolonged P-R interval.

L. N. K.

Koch, Eb.: A Scheme for Electrocardiography. Ztschr. f. Kreislaufforsch. **28**: 200, 1936.

A chart is presented showing the lines of equipotential in a circular electrical field having widely separated large poles in the center. A second circular chart is given of the same diameter, which has three lines radiating from the center at an angle of 120 degrees from each other. When the second chart is superimposed on the first, it will give the values of the potential at the three electrodes and in the three leads correctly in any position. The angle α can also be obtained. The author claims that this procedure is accurate, unlike the trigonometric solution of the Einthoven triangle. The author has not yet made the correction in the case of an eccentrically located bipole.

L. N. K.

Neslin, W.: Autonomic Auricular Rhythm. Wien. Arch. f. inn. Med. **28**: 243, 1936.

The author reports a case in which sinus rhythm coexisted with rhythm discharge from another focus in the auricles. The patient, fifty-three years old, manifested definite evidence of cardiac failure. The electrocardiogram showed sinus arrhythmia, ventricular premature beats, and evidence of intraventricular block. In addition, small waves occurred at regular intervals at a rate of thirty per minute and were not followed by ventricular complexes. They bore no constant time relation to the normal P-waves or the QRS complexes. These regularly recurring waves are interpreted as extrasystolic P-waves arising in a rhythmic focus in the auricles. This focus and the sinus pacemaker acted independently

and each controlled its own portion of the auricles, the two regions being shielded from each other by a region of transient intra-auricular block. The sinus impulse spread to the ventricle, the other did not. The auricles, in this way, were divided into two functionally independent parts.

W. B.

Hadorn, Von W., and Tillmann, A.: Contusion of the Heart. Ztschr. f. Kreislaufforsch. **28**: 185, 1936.

The authors present a case report of a thirteen-year-old girl who, following a severe blow of the chest, developed shock, pain in the upper abdomen, tachycardia, extrasystoles, leucocytosis, transitory S-T and T-wave abnormalities in the electrocardiogram, and an increase in sedimentation rate. This picture following chest injury should lead to the suspicion of contusion of the heart.

L. N. K.

Harrison, T. R., Friedman, Ben, and Resnik, Harry: Mechanism of Acute Experimental Heart Failure. Arch. Int. Med. **57**: 927, 1936.

A method has been described for measuring the coronary blood flow of the dog by means of a cannula passed through the right external jugular vein into the coronary sinus. With this procedure it is possible to calculate the consumption of oxygen and the mechanical efficiency of the heart under various conditions. The sources of error involved have been discussed.

Values are reported for the coronary blood flow and for the work, oxygen consumption, and mechanical efficiency of the hearts of morphinized dogs subjected to no surgical procedure other than the insertion of arterial and venous cannulas. The amount of oxygen consumed by the heart was in general about 10 per cent of that used by the body as a whole. The average value for the mechanical efficiency of the heart was 17 per cent.

An increase in work produced either by increasing the cardiac output or by raising the blood pressure caused an increase in the mechanical efficiency of the heart.

Heart failure produced by chloroform was associated with a decline in arterial blood pressure, in oxygen consumption and in cardiac output. The proportion of the oxygen absorbed by the heart increased, and the mechanical efficiency of the heart diminished. The systemic venous pressure rose only when the animal was moribund. The cardiac output in proportion to the metabolism underwent no constant changes. At autopsy the heart was observed to be dilated, and the lungs were edematous.

Heart failure produced by potassium chloride was associated with a rise in systemic venous pressure, but edema of the lungs did not develop. Constant alterations in the arterial blood pressure, cardiac output, and arteriovenous oxygen difference were not noted. The cardiac consumption of oxygen increased, and the mechanical efficiency of the heart diminished. Dilatation of the heart was a constant postmortem observation.

The observations support the validity of the backward failure (back pressure) theory of the mechanism of heart failure. They are not in accord with the forward failure (diminished output) hypothesis. They demonstrate that in the intact animal, as in the heart-lung preparation, heart failure is characterized by an increase in the volume of the heart and a decrease in the mechanical efficiency.

AUTHOR.

Talley, James E., and Fowler, Kenneth: Tetralogy of Fallot (Eisemenger Type) With Hypoplasia of the Dextroposed Aorta. Am. J. M. Sc. **191**: 618, 1936.

The patient, a woman a little over thirty-one when she died, was born at eight months and was a "blue baby." She had a normal physical and mental develop-

ment, passed through two pregnancies and was able to take care of her house until within a month of her death. The diagnosis of tetralogy of Fallot, with the incompetency of the pulmonary valves, was confirmed post mortem. In addition there was a hypoplasia of both the thoracic and abdominal aorta, which was not suspected.

AUTHOR.

Baker, Thomas, and Shelden, Walter D.: Coarctation of the Aorta With Intermittent Leakage of a Congenital Cerebral Aneurysm. Report of a Case. Am. J. M. Sc. **191**: 626, 1936.

A series of an unusually large number of consecutive necropsies indicates that coarctation of the aorta occurs far more frequently than is clinically appreciated. The pathology and diagnosis of this anomaly is discussed and attention is called to the ease with which this diagnosis may be confirmed or denied. The association of congenital cerebral aneurysm with coarctation is emphasized. A case in which coarctation with possible intermittent leakage of a congenital cerebral aneurysm affected a young woman still living is reported.

AUTHOR.

Leary, Timothy: Atherosclerosis. Arch. Path. **21**: 419, 1936.

All the lesions of aortic atherosclerosis, save the earliest mucoid change, are due to the presence of cholesterol. They are primarily intimal and depend for their nutrition on imbibition through the endothelium. Variation in the character of these lesions is determined by the age of the subject and of the lesions.

In youth cholesterol is introduced into the subendothelial tissue of the intima by globular lipophages or is engulfed by globular lipophages in this situation. Young fibroblastic tissue is produced in the subendothelial tissue, and the young fibroblasts engulf and metabolize the lipoid, leading to its disappearance from the lesions. Repair with minimal scarring follows since the young fibroblastic tissue does not form collagen.

In middle age, cholesterol metabolism within lipoid cells is slowed, the connective tissue forms collagen and scar tissue is produced. There is interference with imbibition of nutriment through the scar tissue, and the deep layers undergo necrosis, with the formation of secondary atheromatous "abscesses" (atherocheumas). Scars are the typical lesions in this period.

In old age, cholesterol metabolism ceases, globular lipophages accumulate in masses, with inadequate nutrition and support, and a primary atheromatous "abscess" (atherocheuma) is the typical lesion.

The lesions of the ascending arch are exceptions to these rules, the metabolism of cholesterol being successfully carried on, as in youth, up to advanced ages. The connective tissue which is formed is reticular, as in youth, and minimal scarring is usual.

Calcification arises in connection with necrobiosis or after necrosis has developed. It is a terminal monumental deposit marking the sites formerly occupied by living tissue.

AUTHOR.

Leary, Timothy: Atherosclerosis. Etiology. Arch. Path. **21**: 459, 1936.

The evidence against cholesterol as etiologic agent is considered first and is found wanting. Leary then, after considering his own and others' evidence for this substance, concludes that the disease atherosclerosis is due to disturbances of cholesterol metabolism. Stresses appear to determine the localization of the lesions.

L. H. H.

Darley, Ward, and Doan, Charles A.: Primary Pulmonary Arteriosclerosis With Polycythemia: Associated With the Chronic Ingestion of Abnormally Large Quantities of Sodium Chlorid (Halophagia). Am. J. M. Sc. **191**: 633, 1936.

The case herewith presented is that of a young female, aged twenty years, who since early childhood had manifested the signs and symptoms of obstruction in the lesser circulation. Autopsy revealed marked pulmonary arteriolar sclerosis, dilatation of the pulmonary artery, and right ventricular hypertrophy.

During most of her life the patient had ingested abnormally large amounts of salt (as much as 3 pounds in one week). No cause for this abnormality could be found. It is of interest that her taste threshold for salt was much lower than the thresholds of persons who were normal in respect to salt desire and intake, that her fluid intake and output were not materially disturbed by variations in salt intake, and that the osmotic pressure and the chemistry of the blood were not altered.

The case is discussed at length from the standpoint of possible causes of arteriosclerosis. Moschcowitz insists that, save with very few exceptions, pulmonary arteriosclerosis is the result of long-standing hypertension in the lesser circulation. Most such cases of hypertension are secondary to congenital abnormalities of the heart or pulmonary vessels or to extravascular or intravascular circulatory obstruction. In this patient we were unable to demonstrate any cause of obstruction or hypertension in the lesser circulation other than the arteriolar hyperplasia itself. Consequently, we consider this case to be one of primary pulmonary arteriosclerosis, and, since microscopic examination of the pulmonary tissue failed to reveal any evidence of syphilitic arteritis, we feel that it should be further classified as one of unknown etiology.

AUTHOR.

Levin, Paul M., and Bucy, Paul C.: Proliferative Endophlebitis (Phlebosclerosis). Report of a Case. Arch. Int. Med. **57**: 787, 1936.

A case of proliferative endophlebitis is presented, which appears to be unique in that the lesions were associated with symptoms definitely indicative of impairment of the venous return.

AUTHOR.

Bitzer, E. W. Observations on the Effect of Sudden Changes in Arterial Tension in Angina Pectoris. Ann. Int. Med. **9**: 1120, 1936.

Sixty-four patients with angina pectoris were subjected to the cold pressor test. Thirty-two cases had normal blood pressures; 27 were hypertensive and five were hypotensive. Fifty-three per cent of the angina pectoris cases with normal blood pressure had a ceiling, or maximal rise, in systolic pressure to 150 mm. or more. The average rise in this group was 29.84 mm. systolic and 16.53 mm. diastolic. The greatest reaction occurred in a hypertensive case, 82 mm. systolic and 45 mm. diastolic. Two cases showed a reverse reaction, a precipitate drop in pressure, with a slowing of the pulse rate, pallor, and sweating about the head.

Electrocardiographic studies were made. A chest lead was taken immediately preceding the test and repeated at the height of the reaction. Twelve cases showed more than 1 mm. change in the QRS and T deflections during the cold pressor test. Four cases showed changes in the R-T segment.

Only one case developed an attack of angina pectoris. This individual was acutely reactive to cold. Handling ice or drinking ice water would immediately precipitate an attack, which could be relieved by immersing the hands in hot water. The carbon dioxide test was used on this patient and caused a similar rise in blood pressure but failed to produce an attack of angina pectoris.

AUTHOR.

Pinkston, J. O., Partington, P. F., and Rosenblueth, A.: A Further Study of Reflex Changes of Blood Pressure in Completely Sympathectomized Animals. Am. J. Physiol. **115:** 711, 1936.

Completely sympathectomized and vagotomized cats and dogs were studied. Reflex rises and falls of blood pressure were obtained on stimulation of afferent nerves and these responses were not abolished by exclusion of the splanchnic vascular area. No significant reflex rises of blood pressure were obtained on occlusion of the innervated carotids. Struggle was attended by a sharp, severe fall of blood pressure in cats but not in dogs. These reactions are at least partly controlled by nonsympathetic vasomotor nerves, which are probably the dorsal root dilators.

E. A.

Albrecht, H.: Pregnancy in Essential Hypertension. Monatschr. f. Geburtsh. u. Gynäk. **100:** 301, 1935.

Pregnancy may aggravate the conditions of the blood vessels in essential hypertension and, also, may lead to nephrosis or eclampsia. These patients, therefore, should be carefully watched.

L. N. K.

Morlock, Carl G., and Horton, Bayard T.: Variations in Systolic Blood Pressure in Renal Tumor: A Study of 491 Cases. Am. J. M. Sc. **191:** 647, 1936.

This analysis shows striking uniformity of the readings of systolic blood pressure for the various histological types of renal tumor. Practically identical incidences for the different groups of blood pressure occurred both in cases of hypernephroma and in those of renal tumors of other types. No consistent alteration in blood pressure occurred following removal of a tumor of either type. This was particularly significant in cases of hypernephroma in which for both males and females as high an incidence of hypertension occurred after removal of the tumor as existed prior to operation. Scrutiny of the males with renal tumors other than hypernephroma would lead one to think that they experienced a diminution of arterial tension following operation, but since an exactly opposite situation existed with respect to the females, we can hardly attach significance to this. In conclusion, we found no constant increase in the blood pressure of patients who were suffering from renal tumors. In particular we failed to substantiate the observation of previous investigators: that a marked fall of an antecedent hypertension followed removal of a hypernephroma. Finally, we would suggest that this study offers clinical evidence that an epinephrine-like pressor substance is not produced by the hypernephromatous type of renal tumor.

AUTHOR.

Barker, Nelson W., and Camp, John D.: Direct Venography in Obstructive Lesions of the Veins. Am. J. Roentgenol. **35:** 485, 1936.

The value of direct venography in obstructive lesions of the veins can be summarized as follows: (1) It may aid in evaluation of disturbances in rate of venous blood flow. (2) It may aid in localizing and determining the extent of an obstructive lesion. (3) It may be of diagnostic aid in obscure cases, particularly when extrinsic obstruction is suspected. The simplicity and safety of the method recommend it. Contraindications are idiosyncrasy to iodides and recent acute thrombophlebitis. The method has definite limitations, but there also are many possibilities for variations, and improvements in technic.

E. A.

Yater, W. M., and Cahill, J. A.: Bilateral Gangrene of Feet Due to Ergotamine Tartrate Used for Pruritus of Jaundice. J. A. M. A. 106: 1625, 1936.

This case report begins with a review in summary of the literature regarding gangrene of the extremities following therapeutic use of ergot preparations. In the present instance the gangrene ensued rapidly upon the dosage of 0.5 mg. ergotamine tartrate hypodermically for six and one-third days. Arteriograms showed a complete occlusion of the main arteries of the leg in the lower one-third. Both lower legs were amputated.

A pathological report of the vessels in the amputated portions is included. The lesion is essentially one of intense arterial constriction, with varying amounts of hyaline degeneration in the vessel walls.

L. H. H.

Gould, S. E., Price, A. E., and Ginsberg, H.: Gangrene and Death Following Ergotamine Tartrate (Gynergen) Therapy. J. A. M. A. 106: 1631, 1936.

A case report of gangrene of both lower legs, and intense peripheral artery involvement in other parts of the body following the subcutaneous injection of four daily doses of ergotamine tartrate totaling 1 mg. The patient died within a day after the last of the four doses had been given.

The drug had been administered as treatment for the pruritus of jaundice following neoarsphenamine therapy. Post-mortem examination showed all the arterioles examined to be contracted.

L. H. H.

Cole, Harold N., and Usilton, Lida J.: Cooperative Clinical Studies in the Treatment of Syphilis. I. Uncomplicated Syphilitic Aortitis: Its Symptomatology, Diagnosis, Progression, and Treatment. Arch. Int. Med. 57: 893, 1936.

The frequency of incidence of uncomplicated syphilitic aortitis is 4.9 per cent in patients admitted to the clinic with latent syphilis or syphilis in the late stage (exclusive of benign late syphilis of the bones or skin and syphilis of the viscera other than the cardiovascular organs). The total number of patients with uncomplicated syphilitic aortitis was 326. The manifestation was observed nearly three times more frequently in negroes than in white patients.

Ten per cent of the patients in whom uncomplicated syphilitic aortitis was detected had had the infection for less than five years.

The Wassermann reaction of the blood was positive in 72 per cent of the cases. There were unquestionable abnormalities of the spinal fluid in 49 per cent of the cases in which examination was made.

Of 935 patients with the early stage of syphilis followed for a period of from three to ten years, cardiovascular syphilis developed in 1.6 per cent; among 105 patients folowed for from ten to twenty years, cardiovascular syphilis developed in 6.7 per cent. However, among the patients who were followed from three to twenty years, none of the graver forms of cardiovascular syphilis developed if treatment had been adequate and regular during the early stages of syphilis.

It was noted that treatment definitely improved the outlook in 267 patients followed for one year or more after the detection of uncomplicated syphilitic aortitis.

The average duration of life in patients who died has been increased from thirty-four to eighty-five months when adequate treatment has been given after the detection of uncomplicated syphilitic aortitis.

Of patients adequately treated after the detection of uncomplicated syphilitic aortitis, 63 per cent were living and free from symptoms, with no progression of the

cardiovascular syphilis, as compared with 49 per cent of those inadequately treated.

Cardiovascular syphilis was definitely or probably the cause of death in 7.9 per cent of the patients inadequately treated after the detection of uncomplicated syphilitic aortitis, as compared with 2.4 per cent of those adequately treated.

The average duration of life for patients who had been treated with small doses of arsenicals was twenty months longer than that for patients who had been treated with large doses.

In cases of uncomplicated syphilitic aortitis it is well to give a preliminary course of injections of a soluble or an insoluble preparation of heavy metal.

AUTHOR.

Cole, Harold N., and Usilton, Lida J.: Cooperative Clinical Studies in the Treatment of Syphilis: Cardiovascular Syphilis. II. Syphilitic Aortic Regurgitation: Its Treatment and Outcome. Arch. Int. Med. 57: 910, 1936.

There were 260 cases of syphilitic aortic regurgitation in the entire group of cases of cardiovascular syphilis. Two hundred and fifty-seven patients were admitted with latent syphilis or syphilis in the late stage (principally with involvement of the cardiovascular or the central nervous system), and an additional 3 patients admitted with syphilis in the early stage were detected during treatment in these clinics.

The frequency of aortic regurgitation in patients who had been under observation or treatment for six months or longer and who were admitted with syphilis in the late stage (principally with involvement of the cardiovascular or central nervous system) or with latent syphilis was 4.1 per cent.

Aortic regurgitation was observed twice as frequently in the negro as in the white patients; the incidence was more than three times higher in negro men than in white men.

Aortic regurgitation was observed most frequently from twenty to thirty years after infection.

The Wassermann reaction of the blood showed some degree of positivity in 85 per cent of the cases in which the test was carried out within ten days of the detection of aortic regurgitation.

In the cases in which a lumbar puncture was done, the spinal fluid of 82, or 62 per cent, showed definite abnormalities.

One of the most interesting facts revealed from these data is that 69 per cent of the patients had had no antisyphilitic treatment prior to that given for aortic regurgitation.

The treatment administered to certain patients who apparently received adequate therapy before the appearance of the aortic regurgitation was found to have been irregularly given after the syphilis was in the late stages.

The average duration of life was increased from forty to fifty-five months with adequate treatment after the detection of the syphilitic aortic regurgitation.

The administration of an adequate amount of both an arsenical and a heavy metal was found to be highly beneficial to patients with syphilitic aortic regurgitation.

From the patients with syphilitic aortic regurgitation or aneurysm who died, the average duration of life was thirty months when congestive heart failure was present before treatment and forty-seven months when congestive heart failure was not present.

Cardiovascular syphilis was the cause of death in 33 per cent of the patients in whom congestive heart failure had been present at some time and in 5 per cent of those in whom it had never been present.

Symptomatic relief was noted in 30 per cent of the patients who had received less than thirteen injections of an arsenical, with an interim course of a heavy metal,

and in 60 per cent of the patients who had received thirteen or more injections of an arsenical, with an interim course of a heavy metal.

A scheme of treatment for use in cases of aortic regurgitation is given.

AUTHOR.

Cole, H. N., and Usilton, Lida J.: Cooperative Clinical Studies in the Treatment of Syphilis: Cardiovascular Syphilis. III. Aneurysm: Its Symptomatology, Diagnosis, Treatment, and Outcome. Arch. Int. Med. 57: 919, 1936.

Seventy-four cases of sacculated aneurysm were included in the study.

In 50 per cent of the cases a saccular aneurysm was observed in the period from fifteen to twenty-five years after the infection, and in three cases, as late as from thirty-five to forty years after infection.

The location of the aneurysm is given in the text. Three patients had three aneurysms each.

The Wassermann reaction of the blood was positive in 90 per cent of the cases in which it was made within ten days of the diagnosis, and in 64 per cent of the cases in which lumbar puncture was made within two months of the diagnosis, there was a definitely abnormal fluid.

Of the total number of patients with aneurysm, 31 per cent showed concomitant involvement of the central nervous system, principally of the parenchymatous type. This percentage represents the minimum, since in a number of cases the gravity of the cardiovascular syphilis precluded the making of a lumbar puncture.

Seventy-seven per cent of the patients had not been treated prior to the detection of the aneurysm.

Of a group of 64 patients with aneurysms, with symptoms on admission, symptomatic relief was obtained in 44 per cent. Symptomatic relief was obtained in 43 per cent of the patients who were not given arsenical therapy as a part of the treatment but who did receive a good course of a heavy metal and potassium iodide, whereas symptomatic relief was gained in 30 per cent of the patients who were given less than thirteen arsenical injections and an interim course of a heavy metal; in 56 per cent of the patients who were given thirteen or more arsenical injections, with an interim course of a heavy metal, symptomatic response was obtained. In all cases comparable forms of medical cardiac regimen were used, regardless of whether antisyphilitic treatment was administered.

Of the seventy-four patients with a saccular aneurysm, 80 per cent were followed for a period of one year or longer after the detection of this involvement, 30 per cent for five years or longer, and 16 per cent for eight years or longer.

The average duration of life after the detection of the aneurysm of patients receiving an adequate amount of each drug was thirty-seven months, which increased to seventy-five months when adequate antisyphilitic treatment was given.

Among the twenty-two patients who died, there were thirteen who died definitely or presumably of cardiovascular syphilis.

An outline of treatment for patients with aneurysm is suggested.

AUTHOR.

Patterson, Russel H., and Stainsby, Wendell J.: The Therapeutic Effects Following Interruption of the Sympathetic Nerves; Report on the Alcohol Block in Certain Arthritic and Vascular Cases. Ann. Surg. 103: 514, 1936.

Diseases definitely benefited by interrupting the sympathetic nerves are: Raynaud's disease, thrombo-angiitis obliterans, scleroderma, cardiac and aortic pain, and megacolon. The diagnostic procaine block should always be done before an attempt is made to interrupt the sympathetic nerves permanently. Blocking the

sympathetic nerves with alcohol seems to be an excellent substitute for operative procedures, but the technic of blocking should be carried out only after acquiring a thorough knowledge of the anatomy and physiology of the autonomic nervous system and after many trials on cadavers. With the present technic, it is impossible to interrupt all sympathetic nerves to an extremity without interrupting sympathetic nerves to other parts of the body, e.g., blocking the sympathetic nerves to the arm produces Horner's syndrome and also blocks some of the sympathetic pathways to the chest.

E. A.

Plá, Juan Carlos, and Cuoco, Jose A.: Embolism of the Abdominal Aorta. Rev. argent. de cardiol. **2:** 274, 1935.

A case is reported of embolism of the abdominal aorta diagnosed clinically and confirmed by autopsy. The patient was a poorly treated syphilitic, affected also by mitral stenosis and auricular fibrillation. The embolus probably came from the left auricle in which the autopsy showed an organized thrombosis, the lower portion of which appeared irregular and torn off. The diagnosis was established on the basis of the sudden paraplegia with bilateral anesthesia and total absence of arterial pulsation in both lower limbs.

H. McC

Clute, Howard M.: Acute Arterial Obstruction from Arteritis. New England J. Med. **214:** 137, 1936.

From the experience gained in these two cases reported, it appears that resection of part of an occluded artery, as Leriche suggests, has a beneficial effect both on the trophic disturbances in the limb and the establishment of a collateral circulation. Probably the increase in the blood supply following arteriectomy is due to paralysis of the vasomotor nerves to the accessory arteries of the heart. Excellent collateral circulation usually follows a dissection of major arteries in dogs, but gangrene frequently follows simple ligation of the same vessels. Leriche recommends dissection of the obliterated artery for certain painful amputation stumps when the vessels were ligated in continuity, for trophic ulcers on amputation stumps, and for localized arteritis and recent thrombosis in arteriosclerosis. He believes the best results occur when the entire obliterated portion of the artery can be removed, but he does not recommend the procedure in Buerger's disease.

The operative procedure in each of the cases was limited to the removal of but a short piece (2 inches) of the thrombosed vessel. No attempt was made to remove the entire artery. Such a procedure does not seem wise, first, because it does not appear necessary for good results, and, second, because such an extensive dissection might well injure some of the collateral arteries. The end-results in the first case were not so good as in the second case because of the delay in recognition of the condition until the process had advanced well up the brachial artery to involve more of the main arterial trunk. Early interference in the second case gave a better opportunity for the development of a good collateral circulation.

One must be impressed in these two cases with the apparent relation of the sympathetic nerves of a main artery to many of the symptoms and signs which follow its occlusion. From the experience gained, it appears that resection of part of an occluded arterial trunk aids in the establishment of a collateral circulation and overcomes the symptoms arising from the stimulation of the sympathetic nerves of a diseased artery.

AUTHOR.

Capps, Richard B.: A Method for Measuring Tone and Reflex Constriction of the Capillaries, Venules and Veins of the Human Hand With the Results in Normal and Diseased States. J. Clin. Investigation 15: 229, 1936.

A method has been presented for measuring the tone of the veins, venules, and capillaries of the human hand as a whole and for determining the reflex reaction of these vessels to a noxious stimulus, a pinch.

It has been shown that the tone of these vessels normally increases with cold and reflexly increases with the pinch. Their tone decreases with local heat and reflexly with heat to the leg.

Evidence has been presented that the decrease in hand volume following a pinch is actually due chiefly to a reflex constriction of the veins, venules, and capillaries.

In two cases of acrocyanosis an abnormal absence of tone of the veins, venules, and capillaries has been found. Coupled with an unusually slow blood flow at low temperature, this finding can explain the clinical picture.

In two cases of severe malignant hypertension, no significant abnormalities were found by this technic.

AUTHOR.

Loman, Julius, and Myerson, Abraham: Visualization of the Cerebral Vessels by Direct Intracarotid Injection of Thorium Dioxide (Thorotrast). Am. J. Roentgenol. 35: 188, 1936.

The best position for puncture of the carotid artery is the supine with the head hyperextended. In this position the muscles and tissues of the neck are firmly fixed so that the artery may be entered with the least difficulty. The artery is punctured by a number 18 or 19 gauge needle at the level of the cricoid cartilage after initial cleansings of the skin and infiltration of the area with novocaine. When it is apparent beyond a doubt that the needle is within the lumen of the common carotid artery, thorotrast is injected as rapidly as possible while an assistant slows the rate of blood flow through the brain by compressing the homolateral carotid or both internal jugulars. First roentgenographic exposure is made immediately at the completion of the injection and excellent arteriograms are obtained. A fair phlebogram may be obtained by exposing a second film three or four seconds after the first one. In thirty cases no immediate or untoward effects were noted over a period of five months.

It seems probable that in selected cases direct intra-arterial injections of thorotrast will be of definite aid in the diagnosis of certain cerebral conditions, particularly neoplasms and abnormalities of the cerebral vascular tree.

E. A.

Pietrusky: The Question of Vasomotor Disturbances of the Extremities After Electrical Injuries. Deutsch. Gerichtl. Med. 25: 197, 1935.

Most changes in the tissues in death due to electrical injuries can be accounted for as the effects of the electricity on the vessels, such as edema, dilation of the vessels, and localized angiospasms. The dissection of bodies when death was caused by electrical injuries would appear to prove that death is due to a concentration of all the blood in the paralyzed capillary and venous system. An interesting case occurred recently where a patient touching a highly charged electric wire with the right hand received burns on both hands as the current was discharged through the left hand. The injuries healed rapidly, but several months later upon the arrival of cold weather vasomotor disturbances occurred in both upper extremities. It would seem that there is a close connection between an electric injury and disturbed circulation.

J. K.

Battistini, Gaspare: Clinical and Etiopathological Studies of Cyanosis, Particularly in regard to Endocrine and Constitutional Factors. Policlinico (sez. med.) **42**: 480, 1935.

Two sisters developed acrocyanosis at the change of life. The disturbed function of the ovary in connection with a specific constitutional background is responsible for these vasomotor syndromes. Successful hormone therapy seems to prove this theory.

J. K.

McKelvey, G. J.: An Improved Cuff for Use with the Passive Vascular Exercise Unit. J. A. M. A. **106**: 920, 1936.

McKelvey describes a series of soft rubber cuffs for adaptation to various sized thighs, with separate leaves which are compressed on the thigh alternately in the two phases of suction and pressure. They are attached separately to the open end of the boot and to the thigh at the start of each treatment and are claimed to cause no venous congestion.

L. H. H.

Conway, J. H.: Obliterative Vascular Disease. Report of Fifty-One Cases Treated With Passive Vascular Exercise. J. A. M. A. **106**: 1153, 1936.

In this study of the clinical application of alternate suction and pressure in patients, the author states his belief that gradual pressure changes are equally effective with sudden alternation in environmental pressure and that they are without danger of injury to the intima of diseased vessels.

The pavaex apparatus was used. The treatments were centralized in the physical therapy department of the New York Hospital.

Of 36 arteriosclerosis obliterans patients, 29, or 80.5 per cent, were improved. Three patients who experienced pain while under treatment did badly and came to amputation, probably because of a diffuse sclerosis involving the arterioles as well as major arteries.

Ten cases of acute vascular occlusion (embolism, thrombosis) were treated, with encouraging results in 9. Of 4 cases of thromboangiitis obliterans, the treatment was a failure in 3, of doubtful value in one. In no case of the whole series was there conclusive evidence that the procedure had itself caused serious complications.

L. H. H.

Machella, T. E.: The Velocity of Blood Flow in Arteries in Animals. Am. J. Physiol. **115**: 632, 1936.

The velocity of blood flow in arteries may be measured by the insertion in the artery of a short length of nickel wire. If this be connected to a Kelvin-Thompson bridge and be used according to the hot-wire principle developed by Hill, the velocity of blood flow may be measured by variations in resistance. Owing to the small mass of the wire used and the intimate contact with the moving stream, the system is able to follow accurately rapid changes in velocity. The method measures velocity of flow rather than volume flow, though the latter can be estimated if the diameter of the vessel is known. The velocity curves of the carotid and femoral arteries are shown to resemble the pressure curves in these arteries and to differ from one another just as do the pressure curves.

When an animal is in good condition, the systolic velocities observed in the carotid and femoral arteries under dial-morphine anesthesia are usually 50 cm. per second or more. The mean velocities are about 9 cm. per second. Studies of the

velocity in the aorta 2 cm. distant from the aortic valves show that the flow at this point does not decrease to zero during diastole; the reservoir action of the aorta and of the aortic valves proximal to this point must, therefore, be considerable. Study of the velocity changes in the coronary arteries demonstrates that the main flow occurs during systole.

E. A.

Kaplan, T.: Frost-Bite. Am. J. Surg. **32**: 318, 1936.

The pathology of this condition may be due to (1) change in the colloid structure of protoplasm incident to the greatly lowered temperature; (2) vasoconstriction and spasm; (3) reactionary hyperemia and transudation of serum further cutting off blood supply; and (4) rarely, thrombosis.

The clinical manifestations and therapy of frostbite are considered briefly, with several references to the literature, but with no personal findings or results included.

L. H. H.

Koch, Julius: Is the Blood Pressure Regulation on Changing Body Posture Dependent Solely on the Four Known Blood Pressure Nerve Regulators? Ztschr. f. Biol. **96**: 314, 1935.

Denervation of the sensory regions of the root of the aorta and of the carotid sinuses has little effect on the ability of the rabbit to maintain the blood pressure when body posture is changed. The author concludes that there must be receptors in other regions than these which are capable of maintaining the blood pressure under these circumstances.

L. N. K.

Levin, E.: Circulators Quotient in Cardiac InSufficiency. Rev. argent. de cardiol. **2**: 354, 1935.

From the assumption that minute volume of blood and circulatory quotient $\frac{\text{Volemia} \times 60}{\text{Chronemia}}$ change always in the same general sense, the circulatory quotient was determined in twenty-seven cardiac patients, both during decompensation and recompensation, in order to seek the corresponding variations of the minute volume of blood.

The results were irregular. In 16 cases the circulatory quotient was lower during cardiac insufficiency; in 4 cases it showed no appreciable change; and in 7 cases it was higher during decompensation than after recompensation. These findings essentially agree with those of some other investigators.

The view is advanced that the minute volume of blood in cardiac patients depends on the oxygen consumed, the degree of its utilization and the reserve power of the heart. These three factors may act in the same or in different ways. Its value, if taken by itself, gives no information regarding tissue oxygenation. An apparently high minute volume of blood may be insufficient and vice versa.

AUTHOR.

Book Reviews

SYNOPSIS OF DISEASES OF THE HEART AND ARTERIES. By George R. Herrmann, M.D., St. Louis, 1936, The C. V. Mosby Company.

The author refers to this small volume as a handbook and modestly states that it is "an attempt to provide an acceptable indexed epitome of the principles and modern conceptions of cardiologic practice." Actually, its 328 pages contain practically all the useful information found in most larger texts, presented in detail, that is ample for practitioners and students, for whom it is primarily designed. The earlier chapters deal with definitions, criteria, the details of history taking, a discussion of the instruments used in the clinical study of patients, and of the value and limitations of the x-ray and electrocardiograph. These subjects occupy less than a third of the book; the remainder is devoted to a discussion of classification of cardiac diseases, arrhythmias, the diagnosis and treatment of congestive and anginal heart failure, coronary thrombosis, bacterial endocarditis, rheumatic and syphilitic disease, the various types of chronic valvular disease, congenital lesions, and pericarditis. The final chapter is upon diseases of the peripheral vascular system.

The author's standing as a teacher and investigator and his many contributions to our knowledge of cardiovascular disease would be sufficient to guarantee the accuracy of his statements and the soundness of his views. He has, however, clearly indicated in the preface that the book is not a presentation of original work or ideas; it is, rather, a comprehensive survey of the entire field by a competent authority who has lucidly summarized our present knowledge of the subject. There are nearly a hundred illustrations, all of them clear and helpful, and many of them notable for originality. The text is written simply and with admirable clarity. There are doubtless some who will criticize the number of pages devoted to a discussion of valve lesions, but the author is too deeply in sympathy with the modern view of myocardial function to discuss these lesions from the viewpoint of twenty years ago, and his discussion is probably a sane corrective to the extreme views of those who regard valve lesions as wholly unimportant.

It is a pleasure to commend this small book to all practitioners and students who wish a brief, timely, up to date, and authoritative discussion of this field of medicine. It is far superior to any similar volume ever encountered by the present reviewer.

H. M. M.

LE SYNDROME ENDOCRINO-HEPATO-MYOCARDIQUE: SUR UN ASPECT DES CIRRHOSES PIGMENTAIRES. By Etienne Royer de Véricourt, Paris, 1936, Masson et Cie.

This monograph of 140 pages is devoted to a presentation of certain aspects of hemochromatosis which, the author believes, constitutes a new syndrome. This consists of multiple endocrine aplasias, hepatic cirrhosis, diffuse visceral hemosiderosis, and severe myocardial failure of a special type.

L. A. C.